

M8 Electronic Common Technical Document (eCTD) v4.0 Draft Implementation Guide v2.0

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**INTERNATIONAL CONFERENCE ON HARMONISATION OF
TECHNICAL REQUIREMENTS FOR REGISTRATION OF
PHARMACEUTICALS FOR HUMAN USE**

ICH M8 Expert Working Group

**ICH Electronic Common Technical Document (eCTD) v4.0
DRAFT ICH Implementation Guide v2.0**

November 13, 2014

32 **DOCUMENT CHANGE HISTORY**

33

Version	Date	Comments
1.0	5.September.2012	Step 2 for Testing version for Steering Committee Sign-off. Included review comments from FDA Legal review. Included changes from HL7 regarding Copyright statement and Legal Notice.
1.1	17.March.2013	Updated with changes from the Step 2 for Testing lessons learnt activities.
1.2	21.April.2013	Updated with changes from Step 2 for Testing lessons learnt activities and review comments from the M8 participants.
1.3	19.May.2013	Updated with changes from review comments of version 1.2.
1.4	1.August.2013	Updated with changes to the RPS Standard (i.e., reflecting model changes) and reorganized the content to match the flow of the XML structure.
1.5	21.October.2013	Updated with changes from review comments of version 1.4 and changes to reactivation of CoU.
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1.7	23.May.2014	Updated with removal of Compound Documents.
1.8	30.June.2014	Updated with changes for simple document approach and model changes. Updated Appendix 1: Sample Files and Folders for Modules 2-5.
1.9	1.August.2014	Updated with changes from review comments of version 1.8.
1.10	14.September.2014	Updated with changes from vendor review and RPS R2 schema.
1.11	30.September 2014	Updated with changes from review comments of version 1.10. Review Version for M2, HL7 and FDA Lawyer.
1.12	17.October.2014	Updated with Forward Compatibility, revisions from v1.11 review and final draft content for Step 2.
1.13	27.October.2014	Updated with comments on Forward Compatibility from M8, and review comments from M2 and FDA Lawyer.
2.0	13.November.2014	Updated with comments from the M8 participants for Step 2 Sign-off in Lisbon, Portugal.

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177 **NOTICE TO READERS**

178 Sections of this document referencing the HL7 (Version 3) Standard, Regulatory Product
179 Submission Release 2 Normative are used with the publisher's permission. The HL7 Standard
180 (Version 3) Regulatory Product Submission Release 2 Normative is copyrighted by Health Level
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182 **INSTRUCTIONS TO READER**

183 This is a technical document that provides instructions on how to implement the eCTD v4.0
184 specification. The content will be provided in a consistent manner within the document. In
185 addition, the reader may be prompted by visual cues about the context or referenced information
186 being presented in the document.





187 **Document Content**

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

- 191 • XML components
 - 192 ○ The document’s narrative text will be bold, italicized text in camel case, e.g.,
193 *contextOfUse*
194 ○ The XML samples will be as notated below in the XML Snippets section.
- 195 • Concepts without attribution to the standard and/or message
 - 196 ○ A defined concept, e.g., Context of Use is noted in plain text with first letter
197 capitalized.

198
199 The following table provides visual cues that are used in the document.

200 **Table 1: Legend of Symbols used in Document**

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

201
202

203 **Common Abbreviations and Terms**

204 The following table defines some common terms in this document and specific to eCTD v4.0.

Abbreviation/Term	Definition
Class	Class is used in this document to qualify a base level element from the HL7 standard.
Datatype	Datatype is used in this document to qualify elements and attributes that come from a datatype in the HL7 standard.
Document	Document is used in this document to identify a content file representing a document required or provided to be submitted. In the eCTD v4.0 message a document will be represented by a document element referencing the file location and providing a title. The document element will be presented in its context of use. Since a document can be used multiple times, a <i>documentReference</i> element allows a document to be specified for the <i>contextOfUse</i> . Each time the document is used in the same submission unit, that document may have a different <i>contextOfUse</i> . The relationship is provided via the <i>documentReference</i> element. Accordingly, each Context of Use must reference a document.
eCTD	Electronic Technical Document
ESTRI	Electronic Standards for the Transfer of Regulatory Information
HL7	Health Level 7 – International Health Data Standards Development Organization
Payload	The payload schema is the eCTD v4.0 base and it contains all of the elements in eCTD v4.0, including items from the Common Product Model and Common Message Element schema. It is organized with the following three elements in the structure: <i>submissionUnit</i> , <i>submission</i> and <i>application</i> .
RPS	Regulated Product Submission – HL7 standard
XML	Extensible Markup Language

205

206 **XML Snippets**

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

209 **Table 2: Legend for XML Snippets**

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

210

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

- 212
- 213 • The notation of *<!--....notes....>* was used to describe conditions that should be met for an element
 - 214 • The notation *... [Description] ...* was used to indicate when there were additional elements
215 not represented in the XML, but may be present in the actual XML message.

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

218

219 **Location in XML**

220 Each of the elements in this document includes a section named, "Location in XML". The
221 notation included uses the following convention:
222

223 **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.

224
225 For example, the following location shows both notations and is followed by the XML sample.
226

- 227
- 228 • *controlActProcess*>> *subject*>> *submissionUnit*>>*component*>>*priorityNumber*>
229 *contextOfUse*

230 **Element's location in XML**

```
231 <controlActProcess classCode="ACTN" moodCode="EVN">  
232   <subject typeCode="SUBJ">  
233     <submissionUnit  
234       <id root="765be5c9-60c9-40e7-b88a-ec9c149a18a1"/>  
235       <code code="ich sub unit 0" codeSystem="2.16.840.1.113883.3.989.2.2.4.9">  
236         <component>  
237           <priorityNumber value="1000"/>
```

238
239 Note: The priority number is represented in the path as it is a required element. In some cases
240 optional elements will not appear in this notation. The schema will enforce any element
241 sequencing requirements, but not optional elements. For ICH specific required elements, refer to
242 Section 8.2 of this document.

243 **XML Elements Tables**

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

248 **Table 4: Sample XML Element Table**

249 Table Name: <element>.<element 2>

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

250

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

254

255 **Element:** Identifies the XML element

256 **Attribute:** Identifies the XML attribute

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

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

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

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

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

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

270 **1. PURPOSE**

271 This document serves as the implementation guide and a technical specification for the Electronic
272 Common Technical Document (eCTD) v4.0 Modules 2 through 5 using the Regulated Product
273 Submission (RPS) Release 2 Normative.
274



Note to Implementers: This implementation guide will need to be used in conjunction with the Regional/Module 1 Implementation Guide, as the eCTD v4.0 message will be incomplete without all of the contents.

275

276 **2. SCOPE**

277 This document only includes the specification information for eCTD v4.0 Modules 2 – 5 submission
278 contents which are shared across all regions. The eCTD v4.0 Regional/Module 1 content, including
279 the Regional Administrative and Product Information, is not included in this implementation guide.

280 This standard defines the message for exchanging regulatory submission information electronically
281 between Regulatory Authorities and the Pharmaceutical Industry. The XML message provides the
282 ability to describe the contents of the regulatory exchange and all information needed to process the
283 exchange between these two parties.

284 For applicants transitioning from eCTD v3.2.2, there are specific transition message instructions
285 outlined in Section 10 in this document.

286 **2.1 Business Case**

287 Regulated Industry and Regulatory Authorities exchange information to address a variety of
288 regulatory processes. The scope of the ICH activities covers the human pharmaceutical product
289 marketing approval processes. Currently, the marketing application is provided in paper format (i.e.,
290 using the CTD) or electronic (i.e., eCTD). Frequently, when new information is provided, it directly
291 relates to information previously submitted. During the regulatory review process as information is
292 submitted, usually in increments, it is difficult to efficiently process and review new information in
293 light of pre-existing information.

294 The goal of upgrading to eCTD v4.0 is to facilitate the processing and review of electronic regulatory
295 submissions. The following items will be discussed in detail in other sections of this document, but
296 are outlined below as they are the key business drivers for the next major version of eCTD:

- 297 • **Document Reuse** – the ability to submit a document once to a Regulatory Authority and refer
298 to the document by its unique identifier in future submissions if the document is validly
299 retained by the Regulatory Authority¹.
- 300 • **Document and Metadata life cycle** – the ability to manage the versions of documents and/or
301 metadata.
- 302 • **Management of Document Groups** – the ability to group files together based on nature of
303 their use (e.g., clinical study reports)

¹ Refer to applicable Regional/Module 1 Implementation Guides for specifics on document retention of regulatory submissions.

304 **3. BACKGROUND**

305 **3.1 General Background and eCTD History**

306 The specification for the eCTD, developed by the ICH M2 Expert Working Group (EWG), is based
307 upon content defined within the CTD issued by the ICH M4 EWG. The structure and level of detail
308 specified in the CTD was used to define the eCTD structure and content, but the CTD did not
309 describe documents that can be submitted as amendments or variations to the initial application. The
310 eCTD was defined as an interface for industry to agency transfer of regulatory information while at
311 the same time taking into consideration the facilitation of the creation, review, life cycle management
312 and archiving of the electronic submission. The current eCTD specification is v3.2.2.

313
314 In addition, the M2 EWG developed the Study Tagging File (STF) Specification. The STF was
315 developed to identify all of the files associated with a study to provide a mechanism to organize the
316 content within a particular study for Modules 4 and 5. The STF is required in the United States, are
317 not required in Europe, and are not allowed in Japan. The current STF specification is v2.6.1.

318
319 The implementation of the eCTD was done regionally and is described in the next section. Overall
320 the eCTD has been very successful and has facilitated the ability to submit global submissions, but
321 since the implementation of eCTD v3.2.2 there have been a number of change requests and M2
322 developed the next major version requirements in 2009. To address the enhancements to the eCTD
323 specification, the M8 EWG was formed in November 2010 to specifically focus on the development
324 and implementation of eCTD v4.0.

325
326 M8 has been actively working on eCTD v4.0 through the HL7 process to ensure that the RPS
327 message meets ICH requirements. Refer to Section 3.3 for more information on HL7. The RPS
328 model now incorporates both the ICH harmonized (Modules 2 – 5) requirements and the ICH
329 regional requirements. RPS Release 2 passed in September 2014 as a HL7 version 3 Normative
330 Standard.

331 **3.2 Implementation Experience in ICH Regions and Observer Countries**

332 This section provides an overview of previous implementation experience of the eCTD v3.2.2. This
333 history is provided by each ICH Region and Observer Country.

334 **3.2.1 European Union**

335 In the early 1990's work was initiated in Europe to develop specification-based electronic
336 submission, the definitions developed at that time still exist today at national level. The first
337 submission in the DAMOS format (Drug Application Methodology with Optical Storage) was made
338 in 1992 to the German Competent Authority (BfArM). An alternative format, called MANSEV,
339 based on HTML and was developed in France, but was never implemented. These European formats
340 and the work to harmonize at a European Level were superseded by the ICH eCTD specification.

341
342 The ICH eCTD specification was adopted in Europe in 2002 (ICH Step 5), this specification has now
343 been in place for more than 10 years to submit dossiers of medicinal products for human use in
344 electronic format. The number of submissions in this format has slowly increased over time. In 2007,
345 due to the low level of adoption by industry and regulators, a variant format was introduced that
346 follows the CTD structure but does not support life cycle management. This was named the non-
347 eCTD electronic submission format (NeeS) and was considered as a stepping stone towards full

348 eCTD implementation.

349
350 A further step to full implementation of electronic submissions was achieved in 2005 when the EU
351 Heads of Medicines Agencies (HMA) agreed to an EU wide initiative for all EU regulatory
352 Authorities to be ready to accept eCTD submissions by 2010, without mandating electronic signature.
353 The EMA mandated electronic only submissions from 1st July 2008 and eCTD was strongly
354 recommended for the Centralised Procedure applications from 1st July 2009. It became mandatory to
355 submit in eCTD format for the Centralised Procedure on 1st of January 2010. Presumably, by mid-
356 2015 the eCTD format for new applications will become mandatory in the decentralized procedure
357 followed by 1st of January 2017 for new applications in the mutual recognition procedure.

358
359 The agreed strategy will aim for establishing secure, consistent and efficient electronic submission
360 processes for medicinal products for human and veterinary use across the European Medicines
361 Regulatory Network (ERMN or “the Network”), which eCTD v4.0 needs to support in a broader
362 sense.

363 **3.2.2 Japan**

364 Pharmaceuticals and Medical Devices Agency (PMDA) began accepting reference eCTD in 2004 and
365 official eCTD in 2005. The number of eCTD submissions in Japan had slowly increased for several
366 years, but the official eCTD submissions drastically increased after 2009 when eCTD v3.2.2 was
367 implemented. Currently, the majority of new drug applications in Japan are submitted as eCTD.

368

369 **3.2.3 United States**

370
371 Acceptance of eCTD v3.0 submissions began at the United States Food and Drug Administration
372 (FDA) in 2003 when the guideline/specification reached ICH Step 4 and was adopted as an ICH
373 harmonised tripartite guideline. On September 1, 2003, FDA began accepting pilot eCTD submission
374 for evaluation. This acceptance was indicated on August 27, 2003 by the publishing of Memo 27 in
375 the Electronic Submissions Public Docket number FDA-1992-S-0039 and the concurrent publishing
376 of technical specifications for eCTD submissions to FDA.

377
378 On September 13, 2007, FDA published Memo 33 which announced its readiness to accept eCTD
379 format submission for both marketed and research regulatory applications. The memo also withdrew
380 previous guidance that allowed for electronic submission in non-eCTD format. As of January 1, 2008,
381 eCTD v3.2.2 has been the preferred format for electronic regulatory submissions to FDA.

382

383 **3.3 The Framework for the ICH eCTD v4.0**

384 Since ICH's inception in 1990, the ICH process has gradually evolved. Beside the development of
385 Tripartite ICH Guidelines on Safety, Quality and Efficacy topics, work was also undertaken on a
386 number of important multidisciplinary topics, like MedDRA (Medical Dictionary for Regulatory
387 Activities; ICH topic M1) or the CTD (Common Technical Document, ICH topic M4). Starting in the
388 new millennium, the need to expand communication and dissemination of information on ICH
389 Guidelines with non-ICH regions became a key focus, accompanied by the need to facilitate the
390 implementation of ICH Guidelines in ICH's own regions.

391 In the last 10 to 15 years, more and more attention was given to the maintenance of already existing
392 Guidelines as science and technology continued to evolve. The need to leverage with other

393 organisations was also acknowledged, particularly for the development of electronic standards. ICH
394 recognised the benefits afforded by collaboration with international Standards Development
395 Organisations, from the perspective of a larger pool of technical expertise and the promising
396 opportunity to progress ICH standards as global standards. This would also allow for extending the
397 benefits of harmonisation beyond the ICH regions by increasing participation of non-ICH regions in
398 guideline development.

399
400 The most desirable long-term objective is to have one globally used electronic message standard to
401 exchange information on regulated products based on internationally approved and interoperable
402 standards.

403
404 In 2006 a basic process description for the involvement of and collaboration with other SDOs
405 (initially ISO, HL7 and CEN) was drafted, based on the “List of Critical Conditions for the SDO
406 Message Standard Development Process”. During the same meeting, the ICH Steering Committee
407 (SC) approved to progress the E2B (R) and M5 messages development with the SDO consortium to
408 evaluate the SDO process.

409
410 At the ICH meeting in October 2007 in Yokohama, a decision was made to move to the next major
411 version of eCTD specification in collaboration with SDOs instead of making slight revisions to the
412 eCTD specification to a next minor version 3.3.3. During the ICH meeting in June 2008 in Portland,
413 the Steering Committee endorsed that ICH would approach HL7 to discuss options to progress the
414 eCTD Next Major Version through the Joint Initiative, a collaboration of ISO, CEN and HL7. To
415 evaluate the acceptability of the resulting standard, ICH collected and collated requirements from
416 each region into a draft ICH requirements document.

417
418 An ICH Expert Working Group (EWG) and Implementation Working Group (IWG) was established
419 to focus on the next major version of eCTD during the meeting in Fukuoka in November 2010, and
420 the new ICH EWG/IWG M8 met for the first time as a group in June 2011 in Cincinnati.

421
422 M8 presented the concept to develop the eCTD Version 4.0 until Step 2 of the ICH process while also
423 working through the HL7 standards development process to enhance the existing RPS Release 1
424 standard. At this time point, the enhanced HL7 RPS standard would be submitted into an ISO fast
425 track process with the result to become an international adopted ISO Standard. In parallel ICH M8
426 would continue the ICH process with the development of concepts, specifications, guidance and a set
427 of tests to support the implementation of the expected ISO standard. This was planned as Step 3 and 4
428 activities of the ICH process to be in alignment with the publication of the ISO standard based on the
429 HL7 RPS Release 2 Normative standard, and the ICH eCTD v4.0 Implementation Guide.

430

431 **3.4 Advantages of eCTD v4.0**

432 The advantages of moving to eCTD v4.0 is to address the new requirements and/or improvements
433 that were needed based on the implementation and usage of eCTD v3.2.2. In addition to the business
434 drivers, the use of an international information exchange standard is needed in the regulatory
435 environment to ensure that mandates can be issued and standardization enabled for increased
436 consistency across the regulatory authorities with respect to the exchange of regulatory information.
437 The key business advantages for upgrading to eCTD v4.0 are noted below:

438

439 **Harmonized submission unit:** In eCTD v4.0, the harmonized and regional content is consolidated
440 into one exchange message – i.e., all content from Module 1 through Module 5 is contained in one
441 exchange message. The exchange message has one schema that will be used to implement the
442 exchange of information via one submission unit – i.e., an XML file. In addition, since the schema
443 will be shared, it will not need to be submitted with each submission unit.
444

445 **Document reuse:** Once a document has been submitted, eCTD v4.0 will allow for this document to
446 be reused in the same context in a different submission unit, submission or application, reused in a
447 different context in the same submission unit or application, or reused in a different context in a
448 different submission unit or application. This is accomplished by assigning each document with a
449 unique ID that can be referenced anywhere in the Regulatory Authority’s environment.
450

451 **Context of Use life cycle:** The Context of Use concept allows for advanced life cycle management
452 operations. A Context of Use may be replaced by one or more Context of Use elements and vice
453 versa (i.e., many to one) through the context of use life cycle.
454

455 eCTD v4.0 will support the existing “new”, “replace”, and “delete” eCTD life cycle operators;
456 however the support for the “append” operation has been removed from the eCTD v4.0 specification.
457

458 eCTD v4.0 also introduces the ability to apply changes to keyword definition display name values,
459 e.g., drug substance/product names, manufacturers, dosage forms, indication, and excipient without
460 resubmitting the physical files or the Contexts of Use element. Refer to Regional/Module 1
461 Implementation Guide for additional information about changes to keyword definitions.
462

463 **Function of document groups:**

464 In eCTD v4.0, documents are referenced by a Context of Use, which specifies where they are to be
465 inserted into the CTD/eCTD table of contents when presenting a reviewable structure.
466 One use of document groups includes the replacement for Study Tagging Files (STFs) in Modules 4
467 and 5 to organize multiple files relating to a single clinical study as noted in the current eCTD
468 specification (v3.2.2). The STF was developed to address the inability of the XML backbone to
469 provide all the metadata necessary to properly represent studies and to organize clinical study report
470 documentation. In eCTD v4.0, the Context of Use code and Keyword combinations will function to
471 create a group of documents.
472

473 For additional information about the technical implementation, refer to Section 8.
474

475 **3.5 Change Control**

476 The eCTD v4.0 specification is based on the HL7 Regulated Product Submission Standard (RPS),
477 which was developed in the external Standards Development Organization (SDO), Health Level
478 Seven International (HL7) and various stakeholders. Changes to the eCTD v4.0 schema² and
479 resulting Implementation Guide will remain the responsibility of the ICH M8 Implementation

² The schema used for the eCTD v4.0 implementation is maintained by HL7.

480 Working Group (IWG) and will follow the established eCTD change control process. Changes that
481 require modifications to the standard will follow established SDO's change control processes³.

482
483 In accordance with the ICH M8 eCTD EWG & IWG Roles and Responsibilities⁴, ICH M8 EWG
484 must:

- 485 i. Ensure fidelity of ICH-Global and ICH-Regional requirements are maintained through
486 SDO process
- 487 ii. Evaluate new requirements brought into SDO process from outside of ICH and review
488 for utility in ICH regions and that they do not contradict ICH requirements
489

490 Change requests originating outside of the ICH M8 EWG should be brought to the attention of the
491 ICH M8 Rapporteur upon their creation so they may be presented to the full ICH M8 EWG to be
492 evaluated, and given a disposition.

493
494 ICH regions are encouraged to create regional processes for the creation of change requests, creation
495 of supporting documentation, and the submission of change request packages to the ICH M8
496 Rapporteur when there is a need to harmonize change across the regions. These processes may be
497 documented in Regional/Module 1 Implementation Guides and/or other regional change control
498 documents.

499
500 Factors that could affect the eCTD v4.0 schema and Implementation Guide include, but are not
501 limited to:

- 502 • Change in the content of the CTD, either through the amendment of information, at the same
503 level of detail, or by provision of more detailed definition of content and structure
- 504 • Updating standards by SDOs that are already in use within the eCTD
- 505 • Identification of new standards that provide additional value for the creation and/or usage of
506 the eCTD
- 507 • Identification of new functional requirements
- 508 • Experience of use of the eCTD by all parties
509

510 Examples of changes that would affect only eCTD v4.0 are:

- 511 • Changes to Controlled Vocabularies maintained by ICH
512

513 Examples of changes that would be needed to address evolving ICH requirements and that may affect
514 the HL7 standards or vocabularies⁵ (including the Modeling and Methodology (MnM), Infrastructure
515 and Messaging (InM), Vocabulary and the RPS Working Groups) are:

- 516 • Changes to the Reference Information Model
- 517 • Changes to the RPS RMIM and/or referenced CMETs
- 518 • Changes to Controlled Vocabularies maintained by HL7
- 519 • Changes to Data Types used by RPS (Note: that this would also require changes to the ISO
520 Standard, which is completed in conjunction with the HL7 processes)

³ This version of the Implementation Guide references the existing standard, RPS and its change control processes. When an ISO standard is available, this section of the document will be updated.

⁴ M8_eCTD_Concept_Paper.pdf available on the ICH website

⁵ This document references changes that may be needed during the Step 2 or Step 3 to meet the existing or evolving ICH requirements. This may be replaced by other processes in the future.

521 Full details of the ICH change control management process are described in an external document
522 titled, *Change Control Process for the eCTD*⁶. Refer to the Regional/Module 1 Implementation
523 Guide for additional information about changes to the regional implementation information.

524 **4. COMPONENTS OF THE ECTD v4.0**

525 This section will provide a brief overview of the essential components of the eCTD v4.0
526 specification. The essential components include:

- 527 • OIDS and UUIDS (summarized in Section 4.5)
- 528 • Data Types (summarized in Section 4.6)
- 529 • Regional/Module 1 Implementation Guides (summarized in Section 4.7)
- 530 • Files and Folders (detailed information provided in Section 5 and Section 11)
- 531 • Controlled Vocabulary (detailed information provided in Section 6)
- 532 • ICH eCTD v4.0 XML Schema (detailed information provided in Section 7)
- 533 • eCTD v4.0 XML message (detailed information provided in Section 8)
- 534 • Forward Compatibility (detailed information in Section 10)
- 535 • Validation Rules (detailed information in Section 12)

536
537 Note: Reference the ESTR1 Website for complete list of documents in the ICH eCTD v4.0
538 Implementation Package.

539 Each of these components is detailed in the subsequent sections to include specific information about
540 the component's role in the implementation of the specification. In order to compose a complete
541 eCTD v4.0 compliant message, the contents of this implementation guide will need to be
542 complemented by several other documents. The focus of this document is to outline the essential
543 components of the eCTD v4.0 and specifically the information required to compose Modules 2 – 5 of
544 the CTD.

545 **4.1 Files and Folder**

546 The files (i.e., documents referenced in the XML message) will be sent in addition to the XML
547 message. Each file will be organized in a folder structure as outlined for the eCTD v4.0. Each
548 *document.text* element within the eCTD v4.0 XML message will be given a specific directory
549 location i.e., the folders that will be used to organize the physical files if the document is being sent
550 for the first time. For detailed information on this topic, refer to Section 5 below.

551 **4.2 Controlled Vocabularies**

552 Controlled vocabularies are one of the essential components of the eCTD v4.0, which enable
553 interoperability – i.e., clear, unambiguous communications between systems sending and receiving
554 XML messages. For the XML elements that have coded values, a controlled vocabulary will be
555 required to indicate the value of the concept. Each code has a code system. The code system may be
556 managed by ICH, Region or the Applicant.

557 Controlled vocabularies are defined external to the message; a code is used as the identifier to convert
558 the code value into the meaningful terms that will be used in any system that implements the viewing
559 of the information sent in the XML message. The controlled vocabularies are detailed in Section 6
560 and examples are given for the applicable XML components.

⁶ All ICH eCTD change control documentation can be found on the ich.org or estri.org websites.

561 For Controlled Vocabularies that will be maintained by ICH, the Expert Working Groups M8 and M2
 562 will work on establishing governance of the eCTD v4.0 controlled vocabulary⁷. All other controlled
 563 vocabularies will be maintained by each Regulatory Authority or designated External organization.



Consult Regional/Module 1 Implementation Guide for additional information about the maintenance of Regional Controlled Vocabulary identified in Section 6.2 below.

564 **4.3 ICH eCTD v4.0 XML Schema**

565 This section will outline the required schema files for the ICH eCTD v4.0 Message. The schemas are
 566 organized by category and sub-categories in the table below. The schemas below will be provided on
 567 the ESTR I website.

	Major Category	Schema Files	
1	Core Schemas: A common schema set for all HL7 v3 messages	infrastructureRoot-r2.xsd voc-r2.xsd datatypes-rX-cs.xsd iso-21090hl7-r2_datatypes.xsd	Referenced by core schema files: infrastructureRoot.xsd datatypes.xsd datatypes-base.xsd NarrativeBlock.xsd voc.xsd
2	RPS Schema: A schema set for the eCTD v4.0 – RPS compliant message	Interactions: PORP_IN000001UV.xsd Message Type: PORP_MT000001UV01.xsd	Control Act: MCAI_MT700201UV.xsd MCAI_MT900001UV.xsd Transmission: MCCI_MT000100UV.xsd
		Referenced Schema Files	
3	Common Product Model Schema: The Common Product Model schemas referenced by the RPS Schemas.	POCP_MT010100UV.xsd POCP_MT010200UV.xsd POCP_MT010300UV.xsd POCP_MT010400UV.xsd POCP_MT010600UV.xsd POCP_MT020100UV.xsd POCP_MT020200UV.xsd POCP_MT030100UV.xsd POCP_MT030200UV.xsd POCP_MT030300UV.xsd POCP_MT040100UV.xsd POCP_MT050100UV.xsd POCP_MT050200UV.xsd POCP_MT050400UV.xsd	POCP_MT060000UV.xsd POCP_MT060100UV.xsd POCP_MT060200UV.xsd POCP_MT070000UV.xsd POCP_MT070100UV.xsd POCP_MT070200UV.xsd POCP_MT080200UV.xsd POCP_MT080300UV.xsd POCP_MT081100UV.xsd POCP_MT082100UV.xsd POCP_MT090100UV.xsd

⁷ Refer to the ESTR I website for additional information

	Major Category	Schema Files	
4	Common Message Elements Schema: The CMETs referenced by the Common Product model or RPS Schemas	COCT_MT030203UV07.xsd COCT_MT040203UV09.xsd COCT_MT050002UV07.xsd COCT_MT070000UV01.xsd COCT_MT090100UV01.xsd COCT_MT090108UV.xsd COCT_MT090300UV01.xsd COCT_MT090303UV01.xsd	COCT_MT150000UV02.xsd COCT_MT150003UV03.xsd COCT_MT240003UV02.xsd COCT_MT440001UV09.xsd COCT_MT710000UV07.xsd COCT_MT960000UV05.xsd COCT_MT150007UV.xsd

568

569 **4.4 The eCTD v4.0 XML Message**

570 The eCTD v4.0 message is based on the ICH eCTD v4.0 schema and has only been constrained
 571 where noted in this Implementation Guide or the Regional/Module 1 Implementation Guides. There
 572 will be one XML message created for a Submission Unit.



Consult Regional/Module 1 Implementation Guide for additional information about the composition of the XML message.

573 **4.5 OIDS and UUIDS**

574 There are two types of unique identifiers, Object Identifiers (OIDs) and Universally Unique
 575 Identifiers (UUIDs). The subsections below provide additional information on how they are used by
 576 ICH eCTD v4.0. Refer to Regional/Module 1 Implementation Guides for regional use of OIDs or
 577 UUIDs.

578 **4.5.1 Object Identifiers**

579 An OID is a sequence of numbers that uniquely identify an object and represent a hierarchically-
 580 assigned namespace. OIDs are formally defined using the International Telecommunications Union
 581 ASN.1 standard⁸. OIDS are represented as follows:

- 582 • String of digits separated by periods: 2.16.840.1.113883
- 583 • list of named branches: {joint-iso-itu-t(2) country(16) us(840) organization(1) hl7(113883)}

584 The current OIDS for the ICH domain include:

- 585 • ich-estri – 2.16.840.1.113883.3.989
- 586 • ich-estri-msg-stds – 2.16.840.1.113883.3.989.2
- 587 • ich-estri-msg-stds-m8-ectd-step2 – 2.16.840.1.113883.3.989.2.2.4
- 588 • ich-estri-msg-stds-m8-ectd-step2-code-lists – 2.16.840.1.113883.3.989.2.2.4.1

⁸ International Telecommunication Union, x680: Information technology – Abstract Syntax Notation One (ASN.1): Specification of basic notation

589 In ICH eCTD v4.0, OIDs will be used to provide the code system value for each element defined by
590 ICH that requires a code. Each required element with a code will indicate when an OID should be
591 provided. Code systems managed by regions or external organizations will have a registered OID.

592 **4.5.2 Universally Unique Identifiers**

593 A UUID is a hexadecimal number in the form of 8-4-4-4-12, including 32 digits and 4 hyphens.⁹
594 UUIDs are formally defined by ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005.
595 UUIDs are represented as follows:

- 596 • String of digits separated by hyphens: 25635f23-a3a4-4ce0-9994-99c5f074960f

597 In ICH eCTD v4.0, UUIDs will be used for any identifier root attribute value. Each required element
598 with an identifier (e.g., id) will indicate when a UUID should be provided.

599 **4.6 Data Types**

600 Data Types are another essential component of the eCTD v4.0 specification. In order to provide all
601 of the information required in the XML message, the data types are represented as elements and
602 attributes. The data type for the elements and attributes are as follows:

- 603 • Alpha – allowing only alpha characters to be used (e.g., language – en, jp, etc.)
- 604 • Alpha Numeric – allowing alpha, numeric and special characters¹⁰ to be used in a string.
605 XML should follow W3C standards for alpha numeric values.
- 606 • Numeric – only allows numeric characters (e.g., 0 through 9.E+-) to be used in a string for
607 integers and real numbers.
- 608 • Boolean: allows a true or false value to be provided.
- 609 • nullFlavors: these are used when required values need to be left blank. Null flavors are based
610 on HL7 Messaging standard, and constraints will be mentioned for each XML element.
611 Currently, null flavors are not used in eCTD v4.0.



Note: The data types for HL7 RPS are specified by ISO 21090: Health informatics -- Harmonized data types for information interchange, however the usage in the eCTD v4.0 Implementation guide refer to the corresponding XML elements or attributes, and the values follow the simple data types as explained above.

613

614 **4.7 Regional/Module 1 Implementation Guides**

615 The Regional/Module 1 Implementation Guides play a key role in providing the administrative
616 information about the submission. The administrative information is mainly found in Module 1 and,
617 as such, is the main subject of the Regional/Module 1 Implementation Guides.

⁹ International Telecommunication Union, x667: Information technology – Open Systems Interconnection – Procedures for the operation of OSI Registration Authorities: Generation and registration of Universally Unique Identifiers (UUIDs) and their use as ASN.1 object identifier components

¹⁰ See Section 5.2.1 for allowable special characters



Note to Implementers: The information in this ICH eCTD v4.0 Implementation Guide is necessary, but not sufficient for creating the complete XML message for transmission. The Regional/Module 1 Implementation Guides are required to send a complete XML message.

The Regional/Module 1 Implementation Guides will be available through the ICH ESTRI website (<http://www.ich.org/products/electronic-standards.html>).

618

619 **4.7.1 Region-Specific Elements**

620 The elements and business rules that are Region/Country specific will be covered by each of the
621 Regional/Module 1 Implementation Guides, as applicable:

622 • *application*

623 ○ *subject.reviewProcedure*

624 ○ *reference.applicationReference*

625 ○ *holder.applicant*

626 ○ *informationRecipient.territorialAuthority*

627 • *submission*

628 ○ *subject3.regulatoryReviewTime*

629 ○ *subject4.submissionGroup*

630 ○ *subject5.Mode*

631 • *review*

632 ○ *subject1.manufacturedProduct*

633 ○ *subject2.productCategory*

634 ○ *subject3.regulatoryStatus*

635 ○ *holder.applicant*

636 ○ *author.territorialAuthority*

637 • *categoryEvent*

638 ○ *categoryEvent*

639



Consult Regional/Module 1 Implementation Guides for additional information about Region/Country the included elements and for specific conformance and business rules for the relevant elements.

640

641 **4.7.2 ICH Excluded Elements**

642 The following class elements are excluded from ICH eCTD v4.0 and should not be sent in the XML
643 message.

- 644 • *Document*
 - 645 ○ *referencedBy.Keyword*
- 646 • *Submission*
 - 647 ○ *subject1.regulatoryStatus*

648



Consult Regional/Module 1 Implementation Guides for additional information about Region/Country specific excluded elements.

649

650 **4.7.3 Excluded Business Processes**

651 This document will not address any regional business processes. The regional business process(es)
652 may include, but are not limited to the following:

- 653 • **Two-way Communication** – includes information on Regulatory Authority communication
654 with the Applicant.
- 655 • **Dossier Management/Submission Life Cycle** – includes rules for Submission Unit,
656 Submission and Applications.
- 657 • **Submission Units with Multiple Submission components** (e.g., Grouped Submissions and
658 Group Variations) – includes rules for sending submission units that will reference more than
659 one submission component.



Consult Regional/Module 1 Implementation Guides for additional information about Region/Country specific excluded business processes.

660 **5. SUBMISSION CONTENTS, FOLDER AND FILE STRUCTURE**

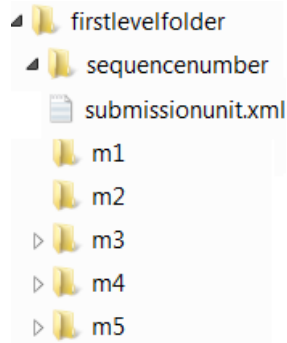
661 The folder and file structure specified for the document contents being transmitted along with the
662 XML message will need to follow various specifications and rules as presented below in this section.

663 **5.1 Submission Unit Contents**

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

665

Figure 1: Submission Unit Folder Structure



666

667 The *First Level Folder* will be determined by Region/Country and additional information can be
668 found in the Regional/Module 1 Implementation Guides.

669 The *Second Level Folder* should be the same for all regions and named with the “*sequence number*”
670 of the submission unit i.e., the actual value of the sequence number e.g., 999 (Refer to
671 Regional/Module 1 Implementation Guides for additional information when there is more than one
672 submission in the submission unit). The following contents should be included in the Second Level
673 Folder:

- 674 • ICH eCTD v4.0 XML Message for an individual Submission Unit, named
675 “submissionunit.xml”. **Note:** the sender should not send the schema files – i.e., the util folder
676 is no longer required, the XML should reference the interaction schema being used, see
677 Section 8.1.
- 678 • Folders for Modules 1 – 5 and the content to be included in that submission unit. The
679 following rules may apply to the contents:
 - 680 ○ Folder structure for m1 folder should follow each Regional/Module 1 Implementation
681 Guide
 - 682 ○ Folder structure for m2-m5 folders should follow the structure provided in this
683 document, see Sections 5.4 and 11.¹¹
 - 684 ○ All files included in these folders should be accounted for in the XML message¹²
 - 685 ○ Files previously sent do not need to be sent again¹³

686 **5.2 Naming Conventions**

687 The naming convention for folders was modified for the eCTD v4.0 implementation. Refer to
688 Section 11 for the complete folder naming conventions for Modules 2-5.

689 Additional guidance for naming convention that is not specified in the sub-sections includes:

- 690 • Folder and file names should be written in lower case only.
- 691 • All files should have one and only one file extension.
- 692 • The file extension should be used to indicate the format of the file.

¹¹ Consult Regional/Module 1 Implementation Guides for any exceptions to this rule.

¹² *Ibid.*

¹³ *Ibid.*

- The First Level Folder should follow details of the respective Regional/Module 1 Implementation Guide.

5.2.1 Allowable Characters

All implementations shall follow the IETF rules for Uniform Resource Locators (URLs) (except for period and asterisk) for file or folder name. The special characters indicated in the table below may be used.

Figure 2: Allowable Special Characters

Special Character	Description
\$	Dollar sign, Peso sign
-	Hyphen, Dash
_	Underscore, understrike, low line, low dash
+	Plus sign
!	Exclamation mark
'	Apostrophe, Single quotation mark
(Left parentheses, Left bracket (UK)
)	Right parentheses, Right bracket (UK)

700



Consult the IETF documentation on *Uniform Resource Identifier (URI)*:

Generic Syntax RFC 3986.

Consult Regional/Module 1 Implementation Guide for a full list of allowable characters.

5.2.2 Length

The restrictions on file or folder name lengths should follow the specifications below:

- Maximum document (i.e., file) name length: 64 (including file name extension)
- Maximum folder name length: 64
- Maximum path length including first level folder: 180
 - *Note: this allows the folder structure to exist under a logical drive with high level folder that is applicable to the submitter's environment*
- File name extension = 3 or 4 characters

5.3 Pathname Conventions and Best Practices

The pathname convention should reference the relative folder path using the forward slash (/) character to separate the folders. For example, the following pathname indicates the location of the file relative to the submissionunit.xml file e.g., "m2/23-qos/introduction.pdf".

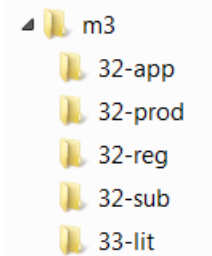


Consult Regional/Module 1 Implementation Guide for additional information on folder path references.

714 5.4 Folder Hierarchy

715 Following the naming and pathname conventions above, the actual physical structure of the folder
716 hierarchy should follow the guidance in Section 11 and Regional/Module 1 Implementation Guide.
717 An example for Module 3 is depicted in the following figure.

718 **Figure 3: Sample Folder Hierarchy of Module 3**



719

720 Refer to Section 11 for the complete folder hierarchy for Modules 2-5.



Note: Sub-folders within a folder should not exceed 25 folders and there should be no more than seven (7) levels of folders (i.e., nesting greater than 6 levels is not acceptable) within the Second-Level Folder.

This allows a cushion before exceeding the limit of 8, as specified by ISO9660. This allows the additional folders that may be needed in the sender or receiver's file directory.

721 5.5 File Formats

722 In the eCTD v4.0 message, file formats are not specified. Consult Regional/Module 1
723 Implementation Guides for additional information about what file formats will be accepted.

724 5.6 Checksums

725 The eCTD v4.0 XML message will contain checksums for all *Document.text.integrityCheck*
726 elements. The SHA-256 integrity check algorithm should be applied to obtain a checksum for all
727 files referenced in a *document* element within a given submission unit.

728 The purpose of the checksum is as follows:

- 729 • The integrity of each file can be verified by comparing the checksum submitted in the XML
730 message and a computed checksum by the receiving system.
- 731 • The checksum can be used to verify that the file has not been altered in the historical archive
732 of the Regulatory Authority.

733 5.7 Compressed Archive

734 A compressed archive is any collection of files that have been added to an archive and the archive has
735 been compressed to minimize the file size of the archive file (e.g., zip files and tar.gz files). There
736 should not be any compressed archives submitted for content in Modules 2 to 5.



Consult Regional/Module 1 Implementation Guides for a full list of allowable file compression archive formats.

737 **6. CONTROLLED VOCABULARIES**

738 As described in Section 4.2, there is extensive use of controlled vocabularies in the execution of an
739 eCTD v4.0 message. The information in the following sub-sections will outline the controlled
740 vocabulary used in developing an eCTD v4.0 message. There are several different authoritative
741 sources for the controlled vocabulary, and as such they are categorized below by the organization that
742 controls the content. The ICH eCTD v4.0-specific terminology – i.e., the controlled vocabulary
743 determined by ICH are listed in Section 6.1.



Note to Implementers: During Step 2, the controlled vocabulary will be provided both as generic code files and spreadsheet format.

744 **6.1 Controlled Vocabularies specified by ICH**

745 The controlled vocabularies specified by ICH M8 for eCTD v4.0 are provided below with a brief
746 description of the terminology and location for obtaining detailed information.

- 747 • eCTD v4.0 – Context of Use Codes: Specifies the code set for the Context of Use values that
748 will represent the headings found in the CTD structure.



Consult Regional/Module 1 Implementation Guide to complete the list of allowable Context of Use vocabulary.

- 749 • eCTD v4.0 – Keyword Codes: Specifies the keyword types that have a controlled vocabulary
750 (e.g., species, route of administration, duration and type of control).



Consult Regional/Module 1 Implementation Guide to complete the list of allowable Keyword Definition vocabulary.

- 751 • eCTD v4.0 – Keyword Definition Codes: Specifies the keyword codes for the types of
752 keywords that are defined by **keywordDefinition** (e.g., manufacturer, dosage form, substance,
753 indication).



Consult Regional/Module 1 Implementation Guide to complete the list of allowable Keyword vocabulary.

754 **6.2 Controlled Vocabularies specified Regionally**

755 The controlled vocabularies specified by each Region for eCTD v4.0 are provided below. The
756 **codeSystem** OIDs for each of the codes sets will be defined in Regional/Module 1 Implementation
757 Guides.

- 758 • eCTD v4.0 – Application Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Application vocabulary.

- 759 • eCTD v4.0 – Application Reference Reason Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Application Reference Reason vocabulary.

- 760
- eCTD v4.0 – Category Event Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Category Event vocabulary.

- 761
- eCTD v4.0 – Contact Party Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Contact Party vocabulary.

- 762
- eCTD v4.0 – Context of Use Codes: Specifies the code set to represent the headings found in the CTD structure that are specified by regional authorities (specifically Module 1).

763



Consult Regional/Module 1 Implementation Guide for a full list of allowable Context of Use vocabulary.

- 764
- eCTD v4.0 – Keyword Codes: Specifies the keyword types that have a controlled vocabulary, which may be additionally specified by regional authorities.

765



Consult Regional/Module 1 Implementation Guide for a full list of allowable Keyword vocabulary.

- 766
- eCTD v4.0 – Keyword Definition Codes: Specifies the keyword codes for the types of keywords that are specified by regional authorities.

767



Consult Regional/Module 1 Implementation Guide for a full list of allowable Keyword Definition vocabulary.

- 768
- eCTD 4.0 – Ingredient Role Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Ingredient Role Code vocabulary.

- 769
- eCTD v4.0 – Manufactured Product Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Manufactured Product vocabulary.

- 770
- eCTD v4.0 – Mode Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Mode vocabulary.

- 771
- eCTD v4.0 – Place Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Place vocabulary.

- 772 • eCTD v4.0 – Product Category Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Product Category vocabulary.

- 773 • eCTD v4.0 – Regulatory Status Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Regulatory Status vocabulary.

- 774 • eCTD v4.0 – Regulatory Review Time codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Regulatory Review Time vocabulary.

- 775 • eCTD v4.0 – Review Procedure Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Review Procedure vocabulary.

- 776 • eCTD v4.0 – Submission Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Submission vocabulary.

- 777 • eCTD v4.0 – Submission Unit Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Submission Unit vocabulary.

- 778 • eCTD v4.0 – Substance Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Substance vocabulary.

- 779 • eCTD 4.0 – Territorial Authority Role Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Territorial Authority Role Code vocabulary.

- 780 • eCTD 4.0 – Territorial Codes



Consult Regional/Module 1 Implementation Guide for a full list of allowable Territorial Code vocabulary.

781 6.3 Controlled Vocabulary specified by HL7

782 The controlled vocabularies specified by Health Level 7 (HL7) are provided below with a brief
783 description of the terminology and location for obtaining detailed information.

- 784 • **HL7 Document Type Codes:** This vocabulary is provided in the HL7 version 3 Standard for
785 the *typeCode* attribute on certain elements within the XML message. These codes are only
786 required for *typeCode* attributes that are not fixed in the XML Schema. The *codeSystem* OID
787 (2.16.840.1.113883.5.1002) is not required in the XML message for any *typeCode* attribute.
- 788 • **HL7 Status Codes:** This vocabulary is provided in the HL7 version 3 Standard for the
789 *statusCode* element part on various elements within the XML message. These are values that
790 should be used in the XML message for *statusCode.code*. The *codeSystem* OID is not
791 required for the statusCodes. Note: Status codes can only use the values provided by HL7
792 (e.g., *codeSystem* OID: 2.16.840.1.113883.5.14).¹⁴
793



Note to Implementers: The controlled vocabulary required by the HL7 RPS standard enables system to system communications and is not always the ideal way to display concepts in a system graphical user interface (GUI). Be cautious not to apply the technical codes in the GUI, instead use the business friendly terms that are specified by Regulatory Authorities in the Regional/Module 1 Implementation Guides.

794 6.4 Controlled Vocabulary specified by Others

795 The controlled vocabulary specified by other organizations (i.e., not managed by ICH, Region or
796 HL7) are provided below noting the responsible organization, a brief description of the terminology
797 and location for obtaining detailed information.

- 798 • **International Organization for Standardization (ISO) - Two-Letter Language Code:** This
799 is a two letter code that is specified for the language as specified in the ISO 639.1 standard.
800 This vocabulary is used to define the *text@language* attribute. The *codeSystem* OID for two-
801 letter language code is 1.0.639.1.
- 802 • **ISO Country Code – Two-letter Country Code:** This is the Country code that is specified in
803 the ISO 3166-1 standard. The *codeSystem* OID for the two-letter Country code is
804 1.0.3166.1.2.2.

805 7. ICH eCTD v4.0 XML SCHEMA

806 7.1 Core Schema

807 The core schemas will be the foundation for the ICH eCTD v4.0 XML schema. These schemas will
808 not be referenced directly, but indirectly by each other and in the referenced ICH eCTD v4.0
809 schemas.

810 7.1.1 InfrastructureRoot-r2

811 This schema defines the properties that are valid for all elements in all other schemas.

812 Note: The elements in this schema are not directly referenced in this implementation guide.

¹⁴ The allowable value set varies by element in the HL7 RPS R2 standard, for specifics of the ICH eCTD v4.0 Implementation, consult the controlled vocabulary artifacts.

813 **7.1.2 iso-21090hl7-r2_datatypes**

814 This schema provides the ISO-21090 datatypes, which are used to define the elements and attributes.
815 This file defines the composition of the ISO-21090 datatypes within the schema and is included in the
816 infrastructure root schema.

817 Note: The elements in this schema are not directly referenced in this implementation guide.

818 **7.1.3 Voc-r2**

819 This schema provides the vocabulary items that are part of the standard. This includes all vocabulary
820 fixed or constrained within the eCTD v4.0 XML schema.

821 Note: The elements in this schema are not directly referenced in this implementation guide.

822 **7.2 eCTD v 4.0 Schema**

823 The eCTD v4.0 schema is composed of schemas that are categorized as Interaction or Message Type.
824 The relevant eCTD v4.0 schemas are presented in this section.

825 **7.2.1 eCTD v 4.0 Interaction Schema**

826 The interaction schema includes three components necessary for a complete XML message, an
827 interaction schema, transmission wrapper schema and a control act schema. Although they are
828 described in this section, further details will be provided in the Regional/Module 1 Implementation
829 Guides.

830 **7.2.1.1 Submission Unit Sent (PORP_IN000001UV.xsd)**

831 This schema is to be used for all eCTD v4.0 interactions for sending submission units from the sender
832 to the receiver. This schema indicates the message type – i.e., primary payload schema and required
833 transmission wrappers.

834 **7.2.1.2 Transmission Wrapper (MCCI_MT0001000UV01.xsd)**

835 This schema provides the transmission wrapper, which is required for all eCTD v4.0 messages. This
836 provides information about the sender and receiver to enable acknowledgements of the individual
837 message.

838 Note: Only the required elements in this schema are mentioned in this implementation guide. Refer
839 to Section 8.1 for required elements.

840 **7.2.1.3 Control Act Wrapper (MCAI_MT700201UV01.xsd)**

841 This schema provides the Trigger Event Control Act for the message being sent.

842 **7.2.1.4 Control Act (MCAI_MT900001UV01.xsd)**

843 This schema provides a mechanism to detect issues in the Control Act Wrapper.

844 **7.2.2 eCTD v4.0 Payload Schema**

845 **7.2.2.1 Payload - Message Type (PORP_MT000001UV01.xsd)**

846 This schema is the eCTD v4.0 base and it contains all of the elements in eCTD v4.0. This schema
847 references many other schemas noted in the section above, including items from the Common
848 Product Model and Common Message Element schema. The referenced schema is not described in
849 this document, nor will they be accessed directly by implementers.

850 8. ECTD v4.0 XML MESSAGE

851 The eCTD v4.0 XML message is composed of more concepts than defined in this section of the
852 implementation guide; this section highlights only the components that are required for Modules 2-5
853 of the CTD.

854 8.1 Message Header

855 The message header information provides a set of elements that are needed to specify the sender and
856 receiver.

857 8.1.1 Sample XML

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

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 ../../schema/PORP_IN000001UV.xsd">  
  <id/>  
  <creationTime/>  
  <interactionId/>  
  <processingCode/>  
  <processingModeCode/>  
  <acceptAckCode/>  
  <receiver typeCode="RCV">  
    <device classCode="DEV" determinerCode="INSTANCE">  
      <id/>  
    </device>  
  </receiver>  
  <sender typeCode="SND">  
    <device classCode="DEV" determinerCode="INSTANCE">  
      <id/>  
    </device>  
  </sender>  
  <controlActProcess classCode="ACTN" moodCode="EVN">  
    <subject typeCode="SUBJ">
```

860

861 8.1.2 Required Elements

862 The schema requires a minimum set of information, including the following:

- 863 • **ITSVersion** must provide the value of “XML_1.0”
- 864 • **xmlns** must have the value “urn:hl7-org:v3”
- 865 • **xmlns:xsi** must have the value “http://www.w3.org/2001/XMLSchema-instance”
- 866 • **xsi:schemaLocation** must have the relative path for the current schema file “urn:hl7-
867 org:v3../../schema/PORP_IN000001UV.xsd”¹⁵
- 868 • **receiver@typeCode** must have the value of “RCV”
- 869 • **receiver.device@classCode** must have a value of “DEV”

¹⁵ The exact schema location will be provided in the Regional/Module 1 Implementation Guides.

- 870 • *receiver.device@determinerCode* must have a value of “INSTANCE”
- 871 • *sender@typeCode* must have the value of “SND”
- 872 • *sender.device@classCode* must have a value of “DEV”
- 873 • *sender.device@determinerCode* must have a value of “INSTANCE”
- 874 • *controlActProcess@classcode* must have a value of “ACTN”
- 875 • *conrtolActProcess@moodCode* must have a value of “EVN”
- 876 • *controlActProcess.subject@typecode* must have a value of “SUBJ”
- 877

878 The following elements are not required by the schema, and may be required by a specific
879 Region/Country. Refer to the Regional/Module 1 Implementation Guides for additional information
880 about these elements:

- 881 • *id*
- 882 • *creationTime*
- 883 • *interactionId*
- 884 • *processingCode*
- 885 • *processingModeCode*
- 886 • *acceptAckCode*
- 887 • *receiver.device.id*
- 888 • *sender.device.id*

889 **8.2 Payload Message**

890 The following eCTD v4.0 XML message components are based on the HL7 Version 3 RPS Release 2
891 Normative. The information for each element is provided in discrete sections, i.e., they are not nested
892 in the same structure of the XML Schema.

893 The following table provides a breakdown of the eCTD v4.0 XML structure with all elements in the
894 XML Schema. The table is organized with the following three elements in the structure:
895 *submissionUnit*, *submission* and *application*. The elements are annotated with balloon text boxes
896 that provide references to either this document (highlighted in blue and referenced by Section
897 number) or Regional/Module 1 Implementation Guides (not highlighted and noted as Regional) to
898 identify the authoritative source of information for the element.

899
900

Table 5: XML Structure

XML Structure	
<p>The eCTD v4.0 begins by identifying the <i>subject</i> element of the XML message. The payload message starts with the <i>submissionUnit</i> element and relates the rest of the elements to the Submission Unit being sent. The <i>submissionUnit</i> element contains the following elements and their attributes:</p> <ul style="list-style-type: none"> • <i>component.contextOfUse</i> <ul style="list-style-type: none"> ○ <i>replacementOf.relatedContextOfUse</i> ○ <i>derivedFrom.documentReference</i> ○ <i>subjectOf.submissionReference</i> ○ <i>referencedBy.keyword</i> ○ <i>primaryInformationRecipient.TerritorialAuthority</i> • <i>componentOfI.submision</i> 	
<pre> <subject typeCode="SUBJ"> <submissionUnit> <id></id> <code></code> <title></title> <statusCode></statusCode> </component> <priorityNumber value=""/> <contextOfUse> <id></id> <code></code> <statusCode></statusCode> <primaryInformationRecipient> <territorialAuthority> <governingAuthority> </governingAuthority> </territorialAuthority> </primaryInformationRecipient> <replacementOf typeCode="RPLC"> <relatedContextOfUse> <id></id> </relatedContextOfUse> </replacementOf> <derivedFrom> <documentReference> <id></id> </documentReference> </derivedFrom> <subjectOf negationInd=""> <submissionReference> <id xsi:type="DSET_II"> <item></item> </id> </submissionReference> </subjectOf> </pre>	<ul style="list-style-type: none"> submissionUnit (Section 8.2.1) Regional/Module 1 Implementation Guides, also included in this document priorityNumber (Section 8.2.4) ICH eCTD v4.0 Implementation contextOfUse (Section 8.2.5) ICH eCTD v4.0 Implementation Guide primaryInformationRecipient.territorialAuthority Regional/Module 1 Implementation Guides replacementOf.relatedContextOfUse (Section 8.2.6) ICH eCTD v4.0 Implementation Guide derivedFrom.documentReference (Section 8.2.7) ICH eCTD v4.0 Implementation Guide submissionReference Regional/Module 1 Implementation Guides

XML Structure	
<pre> <referencedBy typeCode="REFR"> <keyword> <code></code> </keyword> </referencedBy> </contextOfUse> </component> </pre>	<div style="border: 1px solid blue; border-radius: 10px; padding: 5px; width: fit-content;"> <p>Keyword (Section 8.2.8) <u>ICH eCTD v4.0</u> <u>Implementation Guide</u></p> </div>
<p>This section of the XML relates to specifying the Submission element. The following elements may follow the Submission: Note: All of these elements are not included in this implementation guide. Refer to the Regional/Module 1 Implementation Guides for additional information.</p> <ul style="list-style-type: none"> • sequenceNumber (included as an element of the relationship between submissionUnit and Submission) • callbackContact.contactParty • subject2.review • subject3.regulatoryReviewTime • subject4.submissionGroup • subject5.mode 	
<pre> <componentOf1> <sequenceNumber></sequenceNumber> <submission> <id></id> <code></code> <callbackContact> <contactParty> <id></id> </contactParty> </callbackContact> <subject2> <review> <subject1> <regulatoryStatus> <code></code> </regulatoryStatus> </subject1> </review> </subject2> <subject3> <regulatoryReviewTime> <code></code> </regulatoryReviewTime> </subject3> <subject4> <submissionGroup> <id></id> </submissionGroup> </subject4> <subject5> <mode> <code></code> </mode> </subject5> </submission> </componentOf1> </pre>	<div style="display: flex; flex-direction: column; gap: 10px;"> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>sequenceNumber.submission (Section 8.2.2)</p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>submission <u>Regional/Module 1 Implementation Guides</u></p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>callbackContact <u>Regional/Module 1 Implementation Guides</u></p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>review <u>Regional/Module 1 Implementation Guides</u></p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>regulatoryStatus <u>Regional/Module 1 Implementation Guides</u></p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>regulatoryReviewTime <u>Regional/Module 1 Implementation Guides</u></p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>submissionGroup <u>Regional/Module 1 Implementation Guides</u></p> </div> <div style="border: 1px solid black; border-radius: 10px; padding: 5px;"> <p>mode <u>Regional/Module 1 Implementation Guides</u></p> </div> </div>

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

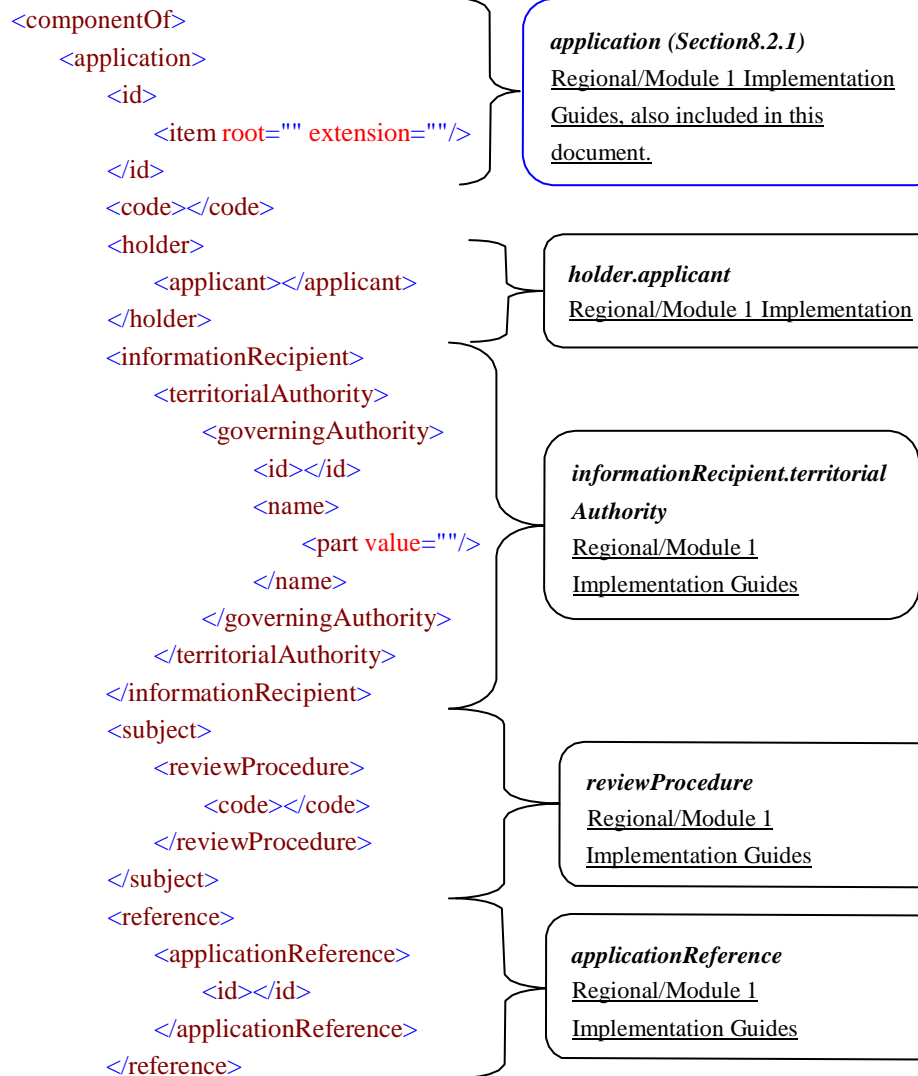
subject.reviewProcedure

reference.applicationReference

component.document

referencedBy.keyword

referencedBy.keywordDefinition



XML Structure

document (Section 8.2.11)
ICH eCTD v4.0
Implementation Guide

keyword
Excluded from ICH eCTD
v4.0 Implementation.

keywordDefinition
(Section 8.2.16)
ICH eCTD v4.0
Implementation Guide

```

<component>
  <document>
    <id></id>
    <title></title>
    <text integrityCheckAlgorithm="SHA256" value=""
      language="">
      <reference value=""/>
    <integrityCheck></integrityCheck>
  </text>
  <referencedBy>
    <keyword>
      <code></code>
      <statusCode></statusCode>
    </keyword>
  </referencedBy>
</document>
</component>
<referencedBy>
  <keywordDefinition>
    <code></code>
    <statusCode></statusCode>
    <value >
      <item>
        <displayName></displayName>
      </item>
    </value>
  </keywordDefinition>
</referencedBy>
  
```

These are the closing element tags for the key elements in the eCTD v4.0 message. The submission unit's category Event is found after the closing tag for the submission, the *componentOf2.CategoryEvent* (and sub category with *component.CategoryEvent*).

```

    </application>
    </componentOf>
  </submission>
</componentOf1>
</componentOf2>
  <categoryEvent>
    <code></code>
    <component>
      <categoryEvent>
        <code></code>
      </categoryEvent>
    </component>
  </categoryEvent>
</componentOf2>
</submissionUnit>
</subject>
</controlActProcess>
</PORP_IN000001UV>
  
```

subject.CategoryEvent
Regional/Module 1
Implementation Guides

902 All information in this section is organized in order that the eCTD v4.0 XML components appear
 903 within the schema.

904 **8.2.1 Submission Unit**

905 The Submission Unit is a collection of documents provided to the Regulatory Authority at one time.
 906 The *submissionUnit* element indicates the information about an individual eCTD v4.0 XML message
 907 – i.e., only one submission unit can be sent at a time.



*Note: **submissionUnit** is primarily a Module 1 concept that will also be provided in the Regional/Module 1 Implementation Guide.*

908 **8.2.1.1 Location in XML**

909 The *submissionUnit* element in the XML message is in the following location:

- 910 • *controlActProcess* >> *subject* >> *submissionUnit*

911 Refer to Table 5: XML Structure for the XML representation.

912 **8.2.1.2 XML Elements**

913 The following tables provide a complete set of XML elements and attributes required for the
 914 *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.

915
 916 Conditions that apply to the *submissionUnit* element:

- 917 • Only one *SubmissionUnit* element can exist for a message.

918 **8.2.1.2.1 *submissionUnit.id***

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>id</i>		[1..1]		This is the container element that uniquely identifies the submission unit sent in the message.
	<i>root</i>	[1..1]	Valid UUID	This is the <i>root</i> attribute that uniquely identifies the submission unit.
<i>Conformance</i>	The <i>id@root</i> is a required attribute.			
<i>Business Rules</i>	The <i>id@root</i> should be unique for every <i>submissionUnit</i> .			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Excluded Elements and/or Attributes</i>				The following datatype attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>id@extension</i> • <i>id@identifierName</i> • <i>id@scope</i> • <i>id@reliability</i> • <i>id@displayable</i> • <i>id@validTimeLow</i> • <i>id@validTimeHigh</i> • <i>id@controlInformationRoot</i> • <i>id@controlInformationExtension</i> • <i>id@nullFlavor</i> • <i>id@flavorId</i> • <i>id@updateMode</i>

919 **8.2.1.2.2** *submissionUnit.code*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is the container element for a code that will define the contents of a submission unit.
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., Original, Amendment, Presubmission</i>	This is the code attribute, which is a value that indicates the type of content in the <i>submissionUnit</i> based on regional controlled vocabulary (e.g., original).
	<i>codeSystem</i>	[1..1]	Valid OID	This is the <i>codeSystem</i> OID that is a unique identifier for the controlled vocabulary system.
<i>Conformance</i>	The <i>code</i> and <i>codeSystem</i> attributes are required.			
<i>Business Rules</i>	For <i>submissionUnit</i> codes consult the Regional/Module 1 Implementation Guides.			

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>code.displayName</i> • <i>code.originalText</i> • <i>code.translation</i> • <i>code.source</i> • <i>code@codeSystemName</i> • <i>code@codeSystemVersion</i> • <i>code@valueSet</i> • <i>code@valueSetVersion</i> • <i>code@codingRationale</i> • <i>code@validTimeLow</i> • <i>code@validTimeHigh</i> • <i>code@controlInformationRoot</i> • <i>code@controlInformationExtension</i> • <i>code@nullFlavor</i> • <i>code@flavorId</i> • <i>code@updateMode</i>

920 **8.2.1.2.3** *submissionUnit.title*

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>title</i>		[0..1]		This is the container element for a user-specified value that describes the contents of a submission unit.
	<i>value</i>	[0..1]	Alpha Numeric <i>Sender specified description – e.g., Presubmission</i>	This is the <i>value</i> attribute of the <i>title</i> element, which provides a string value for the submission unit description.
<i>Conformance</i>	The <i>title</i> is an optional element.			
<i>Business Rules</i>	The <i>title</i> is a sender-specified value that describes the purpose of the submission unit.			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>title.data</i> • <i>title.xml</i> • <i>title.reference</i> • <i>title.integrityCheck</i> • <i>title.thumbnail</i> • <i>title.description</i> • <i>title.translation</i> • <i>title@mediaType</i> • <i>title@charset</i> • <i>title@language</i> • <i>title@compression</i> • <i>title@integrityCheckAlgorithm</i> • <i>title@validTimeLow</i> • <i>title@validTimeHigh</i> • <i>title@controlInformationRoot</i> • <i>title@controlInformationExtension</i> • <i>title@nullFlavor</i> • <i>title@flavorId</i> • <i>title@updateMode</i>

921 **8.2.1.2.4** *submissionUnit.statusCode*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>statusCode</i>		[0..1]		This is the container element that indicates the status of the submission unit.
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., active, suspended*</i> *Consult <i>Regional/Module 1 Implementation Guide</i>	This is the <i>code</i> attribute of the <i>statusCode</i> element, which indicates the status of the submission unit.
<i>Conformance</i>	If the <i>statusCode</i> element is provided, the <i>code</i> attribute is required.			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Business Rules</i>				Refer to Regional/Module 1 Implementation Guides for more information about the use of <i>submissionUnit.statusCode</i> .
<i>Excluded Elements and/or Attributes</i>				The following datatype elements and attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>statusCode.part</i> • <i>statusCode@validTimeLow</i> • <i>statusCode@validTimeHigh</i> • <i>statusCode@controlInformationRoot</i> • <i>statusCode@controlInformationExtension</i> • <i>statusCode@nullFlavor</i> • <i>statusCode@flavorId</i> • <i>statusCode@updateMode</i>

922

8.2.1.3 Terminology



All terminology will be provided as generic code files or in a spreadsheet for Step 2.¹⁶

923

8.2.1.4 Excluded Elements

924 No class elements are excluded for the *submissionUnit* element. Refer to Regional/Module 1
925 Implementation Guides for more information.

8.2.2 Sequence Number

927 The *sequenceNumber* is an increasing numeric value used to maintain a sequential and chronological
928 order within the submission or across submissions; and it is unique within an Application.

8.2.2.1 Location in XML

930 The *sequenceNumber* element in the XML message is in the following location:

931 • *controlActProcess* >> *subject* >> *submissionUnit* >> *componentOf* >> *sequenceNumber*

932 There may be *subject* and *component* elements (specifically in that order) prior to the *componentOf*
933 element.

934 Refer to Table 5: XML Structure for the XML representation.

8.2.2.2 XML Elements

936 The following table provides a complete set of XML elements and attributes required for the
937 *componentOf.sequenceNumber* element, and any special instructions.



The *typeCode* is not required in the eCTD v4.0 XML message. The *typeCode* is fixed to “COMP”. If the XML message contains any other value for this attribute it will be invalid against the schema.

¹⁶ Final Implementation Terminology will be provided on the ESTR1 website.

938 **8.2.2.2.1** *sequenceNumber*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>sequenceNumber</i>		[1..1]		This is the container element for the sequence number and its value.
	<i>value</i>	[1..1]	Numeric <i>e.g., 1, 2, 3.</i>	The <i>value</i> attribute of the <i>sequenceNumber</i> element provides a whole number to be used to order Submission Unit's within a Submission element.
<i>Conformance</i>	<i>sequenceNumber@value</i> attribute is required.			
<i>Business Rules</i>	The <i>sequenceNumber</i> is a positive integer. The values should begin with "1" and increment by whole numbers. The value should not be greater than "999999".			
<i>Excluded Elements and/or Attributes</i>	<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>sequenceNumber@controlInformationExtension</i> • <i>sequenceNumber@controlInformationRoot</i> • <i>sequenceNumber@flavorId</i> • <i>sequenceNumber@nullFlavor</i> • <i>sequenceNumber@uncertaintyType</i> • <i>sequenceNumber@validTimeHigh</i> • <i>sequenceNumber@validTimeLow</i> • <i>sequenceNumber.expression</i> • <i>sequenceNumber.originalText</i> • <i>sequenceNumber.uncertainty</i> • <i>sequenceNumber.uncertainRange</i> 			

939 **8.2.2.3** *Terminology*



There is no controlled terminology for this element.

940 **8.2.2.4** *Excluded Elements*

941 No class elements are excluded for the *sequenceNumber* element.

942 **8.2.3** **XML SAMPLES: Submission Unit**

943 The following is an example of the submission unit element and the specific attributes possible for all
944 submission units.

945 <subject typeCode="SUBJ">
946 <submissionUnit>
947 <id root="0d84467e-f20b-42ad-a69a-63e61a4f7ea7"/>
948 <code code="ich submission unit type 1" codeSystem="2.16.840.1.113883.3.989.2"/>
949 <title value="Original Submission for pain medication - acetyl salicylic acid tablets"/>
950 <statusCode code="active"/>.....
951 *[Additional information may appear after the **statusCode** (if one exists), otherwise the **title or***
952 ***code elements**. For example, depending on the type of submission unit the additional*
953 *elements may be available to select from the submission unit– **subject** or **component***
954 *elements]*
955 ...
956 <componentOf1>
957 <sequenceNumber value="1"/>
958 <submission>
959 ...
960 *[Additional information appears for the **submission** element. Specific contents are defined in*
961 *Regional/Module 1 Implementation Guide]*
962 ...
963 <componentOf>
964 ...
965 *[Additional information appears for the **application** element. Specific contents are defined in*
966 *Section 8.2.10 and Regional/Module 1 Implementation Guide]*
967 ...
968 </componentOf>
969 <submission>
970 </componentOf1>
971 <componentOf2>
972 ...
973 *[Additional information appears for the **CategoryEvent** element. Specific contents are defined*
974 *in Regional/Module 1 Implementation Guide]*
975 ...
976 </componentOf2>
977 </submissionUnit>
978 </subject>
979



See [XML Color Legend](#) for color usage.



Note that the *codeSystem* OIDs provided in the sample above are placeholders for Regional Controlled Vocabulary OIDs.



Refer to Regional/Module 1 Implementation Guides for additional information on sequence numbers, specifically when a submission unit contains more than one submission.

980 **8.2.4 Priority Number for Context of Use**

981 The priority number defines the order in which each Context of Use should appear within each eCTD
 982 v4.0 section of a submission unit. The *priorityNumber* element is always required to be provided. In
 983 cases where more than one Context of Use has the same *contextOfUse.code* value, the
 984 *priorityNumber* will be used to display the elements.

985 **8.2.4.1 Location in XML**

986 The *priorityNumber* element in the XML message is in the following location:

- 987 • *controlActProcess* >> *subject* >> *submissionUnit*>> *component*>> *priorityNumber*

988 Refer to Table 5: XML Structure for the XML representation.

989 **8.2.4.2 XML Elements**

990 The following table provides a complete set of XML elements and attributes required for the
 991 *component.priorityNumber* element, and any special instructions.



The *typeCode* is not required in the eCTD v4.0 XML message. The *typeCode* is fixed to “COMP”. If the XML message contains any other value for this attribute it will be invalid against the schema.

992 Conditions that apply to the *priorityNumber* element:

- 993 • If there are multiple instances of Context of Use elements with the same *contextOfUse.code*
 994 value the priority number will allow ordering of those elements within and across submission
 995 units in an application.
- 996 • If Keywords are also provided with the Context of Use, the priority number should be for the
 997 ordering of the Context of Use and Keyword combination.

998 **8.2.4.2.1 priorityNumber**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>priorityNumber</i>		[1..1]		This is the container element for the priority number and its value.
	<i>value</i>	[1..1]	Numeric <i>e.g., 1000,2000, 3000</i>	The <i>value</i> attribute of the <i>priorityNumber</i> provides a whole number to be used for ordering the Context of Use element.
	<i>updateMode</i>	[0..1]	Alpha <i>e.g., R=Replace</i>	The <i>updateMode</i> attribute provides the coded value to indicate if the <i>priorityNumber</i> has been changed for the Context of Use.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Conformance</i>				<i>priorityNumber@value</i> attribute is required.
<i>Business Rules</i>				<p>The priority number is required for each <i>contextOfUse</i> element.</p> <p>The value shall be a positive integer up to 6 digits (i.e., 1 – 999999) for the <i>contextOfUse</i> element with the same Context of Use code value and Keyword code value pair.</p> <p>It is recommended to start with “1000” and intervals of 1000 (e.g., “2000”, “3000”, etc.) for the initial submission of a CoU sharing the same CoU/ keyword code combination. This allows increments of one, tens and hundreds to be used when reordering and/or inserting CoU.</p> <p>The priority number should not be duplicated within the same CoU code and Keyword combinations. Refer to Regional/Module 1 Implementation Guides for additional business rules for priority number conflicts.</p> <p>The priority number will be used to order the Context of Use elements within the same CoU code and keyword combinations when displayed.</p> <p>If the order of the contents needs to be changed, the <i>updateMode</i> attribute should be used to indicate if the <i>priorityNumber</i> has been updated for the purposes of reordering a new CoU (i.e., <i>updateMode</i>="R"). The <i>updateMode</i> should not be used unless the order of an existing Context of Use is being changed – i.e., avoid using update mode if the CoU is not being reordered with a new priority number value.</p> <p>Additional information is provided in Section 8.2.9.</p>

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>priorityNumber@controlInformationExtension</i> • <i>priorityNumber@controlInformationRoot</i> • <i>priorityNumber@flavorId</i> • <i>priorityNumber@nullFlavor</i> • <i>priorityNumber@uncertaintyType</i> • <i>priorityNumber@validTimeHigh</i> • <i>priorityNumber@validTimeLow</i> • <i>priorityNumber.expression</i> • <i>priorityNumber.originalText</i> • <i>priorityNumber.uncertainty</i> • <i>priorityNumber.uncertainRange</i>

999 **8.2.4.3 Terminology**



There is no controlled terminology for this element.

1000 **8.2.4.4 Excluded Elements**

1001 No class elements are excluded for the *priorityNumber* element.

1002 **8.2.5 Context of Use**

1003 The Context of Use defines the relationship between the table of contents heading
1004 (*contextOfUse.code*) and the referenced document to be associated with that heading. The Context of
1005 Use is relevant to the sequence that it was submitted, which may include one or more *submissions*
1006 referenced in the *submissionUnit*.

1007 The Context of Use code and reference to a document (i.e., *documentReference*) will be used to
1008 connect the content of the submission unit to one or more uses in a table of contents.



The contextOfUse element will be repeated as necessary for a submission unit – i.e., there may be many contextOfUse elements in an XML message.



For each contextOfUse element a priorityNumber should always be specified to indicate the order in which the Context of Use should be displayed. The priorityNumber will be used to order the contextOfUse elements that are submitted with the same contextOfUse.code and keyword.code.

1009 **8.2.5.1 Location in XML**

1010 The *contextOfUse* element in the XML message is in the following location:

- 1011 • *controlActProcess>> subject>> submissionUnit>>component>>priorityNumber>*
1012 *contextOfUse*

1013 Refer to Table 5: XML Structure for the XML representation.

1014 **8.2.5.2 XML Elements**

1015 The following tables provide a complete set of XML elements and attributes required for the
 1016 *contextOfUse* element, and any special instructions.



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

1017 Conditions that apply to the *contextOfUse* element:

- 1018 • Zero to many *contextOfUse* elements can be sent in a *submissionUnit*.

1019 **8.2.5.2.1 contextOfUse.id**

Element	Attribute	Cardinality	Value(s) Allowed	Description Instructions
<i>id</i>		[1..1]		This is the container element that organizes the <i>contextOfUse</i> identifier.
	<i>root</i>	[1..1]	Valid UUID	The <i>root</i> attribute of the <i>id</i> element provides a global unique identifier of the <i>contextOfUse</i> .
<i>Conformance</i>	<i>id@root</i> is a required attribute.			
<i>Business Rules</i>	The <i>id@root</i> should be unique for every <i>contextOfUse</i> submitted.			
<i>Excluded Elements and/or Attributes</i>	The following datatype attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>id@extension</i> • <i>id.item@identifierName</i> • <i>id.item@scope</i> • <i>id.item@reliability</i> • <i>id.item@displayable</i> • <i>id@validTimeLow</i> • <i>id@validTimeHigh</i> • <i>id@controlInformationRoot</i> • <i>id@controlInformationExtension</i> • <i>id@nullFlavor</i> • <i>id@flavorId</i> • <i>id@updateMode</i> 			

1020 **8.2.5.2.2** *contextOfUse.code*

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>code</i>		[0..1]		This is the container element for the type of content referenced under the <i>contextOfUse</i> .
	<i>code</i>	[1..1]	Alpha Numeric	The <i>code</i> attribute provides a coded value that indicates the heading and is defined by ICH or Regulatory Authorities.
	<i>codeSystem</i>	[1..1]	Valid OID	The <i>codeSystem</i> attribute provides a unique identifier that indicates the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
<i>Conformance</i>	If the <i>code</i> element is provided, the <i>code</i> and <i>codeSystem</i> attributes must be provided.			
<i>Business Rules</i>	The <i>code</i> element is required when sending the Context of Use. The <i>code</i> element is not required if the <i>contextOfUse.statusCode</i> is inactivated (i.e., status code equals suspended).			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>code.displayName</i> • <i>code.originalText</i> • <i>code.translation</i> • <i>code.source</i> • <i>code@codeSystemName</i> • <i>code@codeSystemVersion</i> • <i>code@valueSet</i> • <i>code@valueSetVersion</i> • <i>code@codingRationale</i> • <i>code@validTimeLow</i> • <i>code@validTimeHigh</i> • <i>code@controlInformationRoot</i> • <i>code@controlInformationExtension</i> • <i>code@nullFlavor</i> • <i>code@flavorId</i> • <i>code@updateMode</i>

1021 **8.2.5.2.3 contextOfUse.statusCode**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>statusCode</i>		[1..1]		This is the container element that has a controlled terminology code that indicates the status of the Context of Use.
	<i>code</i>	[1..1]	<p>Alpha</p> <p><i>e.g., active, suspended*</i></p> <p><i>*Refer to Regional/Module 1 Implementation Guide</i></p>	The <i>code</i> attribute provides a specified value that indicates whether the Context of Use is still relevant or if it has been removed.
<i>Conformance</i>				The <i>statusCode</i> element is always required when a CoU is specified.
<i>Business Rules</i>				The <i>statusCode@code</i> must always be sent in the message.

<i>Excluded Elements and/or Attributes</i>	<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>statusCode.part</i> • <i>statusCode@validTimeLow</i> • <i>statusCode@validTimeHigh</i> • <i>statusCode@controlInformationRoot</i> • <i>statusCode@controlInformationExtension</i> • <i>statusCode@nullFlavor</i> • <i>statusCode@flavorId</i> • <i>statusCode@updateMode</i>
--	--

1022 **8.2.5.3 Terminology**



All terminology will be provided as genericcode files or in a spreadsheet for Step 2.¹⁷



Codes may be further constrained by regulatory authorities, consult the appropriate Regional/Module 1 Implementation Guide.

1023 **8.2.5.4 Excluded Elements**

1024 No class elements are excluded for the *contextOfUse* element.

1025 **8.2.6 Related Context of Use (Context of Use Life Cycle)**

1026 The *relatedContextOfUse* element allows the sender to relate a *contextOfUse* element to one or
 1027 more *relatedContextOfUse* elements. The *replacementOf* relationship is used for tracking the
 1028 life cycle of context of use elements.

1029 **8.2.6.1 Location in XML**

1030 The *relatedContextOfUse* element in the XML message is in the following location:

- 1031 • *controlActProcess>> subject>> submissionUnit>>component>>priorityNumber>*
 1032 *contextOfUse>> replacementOf>> relatedContextOfUse*

1033 Refer to Table 5: XML Structure for the XML representation.

1034 **8.2.6.2 XML Elements**

1035 The following table provides a complete set of XML elements and attributes required for the
 1036 *relatedContextOfUse* element, and any special instructions.



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

1037
 1038 Conditions that apply to the *relatedContextOfUse* element:

¹⁷ Final Implementation Terminology will be provided on the ESTR1 website.

- 1039 • One or more *relatedContextOfUse* elements may be provided in the XML as being replaced
 1040 by the new *contextOfUse*.

1041 **8.2.6.2.1 relatedContextOfUse.id**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>id</i>		[1..1]		This is the container element for a related contextOfUse as referenced by an identifier.
	<i>root</i>	[1..1]	Valid UUID	This is the <i>root</i> attribute of the <i>id</i> element that provides the global unique identifier for the <i>relatedContextOfUse</i> element being replaced.
<i>Conformance</i>	The <i>id@root</i> is a required attribute			
<i>Business Rules</i>	One <i>contextOfUse</i> element can include one or more <i>relatedContextOfUse</i> elements.			
<i>Excluded Elements and/or Attributes</i>	The following datatype attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>id@extension</i> • <i>id@identifierName</i> • <i>id@scope</i> • <i>id@reliability</i> • <i>id@displayable</i> • <i>id@validTimeLow</i> • <i>id@validTimeHigh</i> • <i>id@controlInformationRoot</i> • <i>id@controlInformationExtension</i> • <i>id@nullFlavor</i> • <i>id@flavorId</i> • <i>id@updateMode</i> 			

1042 **8.2.6.3 Terminology**



All terminology will be provided as generic code files or in a spreadsheet for Step 2.¹⁸

¹⁸ Final Implementation Terminology will be provided on the ESTRi website.

1043 **8.2.6.4 Excluded Elements**

1044 No class elements are excluded for the *relatedContextOfUse* element.

1045 **8.2.7 Document Reference**

1046 Since a document can be used multiple times, a *documentReference* element allows a document to be
 1047 specified for the *contextOfUse*. Each time the document is used in the same submission unit, that
 1048 document may have a different *contextOfUse*. Accordingly, each Context of Use must reference a
 1049 document.

1050 **8.2.7.1 Location in XML**

1051 The *documentReference* element in the XML message is in the following location:

- 1052 • *controlActProcess*>> *subject*>> *submissionUnit*>>*component*>>*priorityNumber*>
 1053 *contextOfUse*>> *derivedFrom*>> *documentReference*

1054 There may be one or more *replacementOf* elements prior to the *derivedFrom* element.

1055 Refer to Table 5: XML Structure for the XML representation.

1056 **8.2.7.2 XML Elements**

1057 The following table provides a complete set of XML elements and attributes required for the
 1058 *documentReference* element, and any special instructions.



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

1059 Conditions that apply to the *documentReference* element:

- 1060 • Zero to one *documentReference* elements can be sent for each *contextOfUse*.
- 1061 • For a contextOfUse.statusCode= active – the *documentReference* element is required.
- 1062 • For a contextOfUse.statusCode= suspended – the *documentReference* element should not be
 1063 provided.

1064 **8.2.7.2.1 documentReference.id**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>id</i>		[1..1]		This is the container element for a reference to a Document.
	<i>root</i>	[1..1]	Valid UUID	The <i>root</i> attribute or the <i>id</i> element provides a global unique identifier of the Document being referenced.

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>Conformance</i>				The <i>id@root</i> attribute is required if the <i>documentReference</i> element is provided.
<i>Business Rules</i>				The <i>id@root</i> is a reference to a document sent in the submission unit or a previously submitted submission unit. <i>Note: Refer to applicable Regional/Module 1 Implementation Guide for specifics on document retention of regulatory submissions.</i>
<i>Excluded Elements and/or Attributes</i>				The following datatype attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>id@extension</i> • <i>id@identifierName</i> • <i>id@scope</i> • <i>id@reliability</i> • <i>id@displayable</i> • <i>id@validTimeLow</i> • <i>id@validTimeHigh</i> • <i>id@controlInformationRoot</i> • <i>id@controlInformationExtension</i> • <i>id@nullFlavor</i> • <i>id@flavorId</i> • <i>id@updateMode</i>

1065 **8.2.7.3 Terminology**



There is no controlled terminology for this element.

1066 **8.2.7.4 Excluded Elements**

1067 No class elements are excluded for the *documentReference* element.

1068 **8.2.8 Keyword**

1069 The *keyword* element is used for the purposes of transmitting additional information about a
1070 *contextOfUse*. The *keyword* is either defined by an external controlled vocabulary or it may be
1071 defined within the message as *keywordDefinition*.

1072 **8.2.8.1 Location in XML**

1073 The *keyword* element in the XML message is in the following location for Context of Use:

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

1076 There may be a *primaryInformationRecipient*, *replacementOf*, *derivedFrom*, or *subjectOf* element
1077 prior to the *referencedBy* element.

1078 Refer to Table 5: XML Structure for the XML representation. Note: Document *keyword* elements are
1079 excluded in eCTD v4.0 messages.

1080 **8.2.8.2 XML Elements**

1081 The following table provides a complete set of XML elements and attributes required for the *keyword*
 1082 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 *typeCode* is required in the eCTD v4.0 XML message. The *typeCode* should be to “REFR”. If the XML message contains any other value for this attribute it will be invalid against the schema.

1083 Conditions that apply to the *keyword* element:

- 1084 • Zero to many *keyword* elements can be sent for each *contextOfUse* element.
- 1085 • Consult Regional/Module 1 Implementation Guides for specific types of Keywords that
 1086 should be used with *contextOfUse* elements.

1087 **8.2.8.2.1 keyword.code**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is the container element that identifies the keyword.
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., “M123456” for Manufacture Site</i>	This is the <i>code</i> attribute that identifies the code value for the keyword.
	<i>codeSystem</i>	[1..1]	Valid OID	This is the <i>codeSystem</i> OID that is a unique identifier for the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
<i>Conformance</i>	The <i>code</i> and <i>codeSystem</i> attributes are required. A keyword can only have one code.			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Business Rules</i>				The display name for the <i>code</i> needs to be retrieved from the corresponding code system.
<i>Excluded Elements and/or Attributes</i>				The following datatype elements and attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>code.displayName</i> • <i>code.originalText</i> • <i>code.translation</i> • <i>code.source</i> • <i>code@codeSystemName</i> • <i>code@codeSystemVersion</i> • <i>code@valueSet</i> • <i>code@valueSetVersion</i> • <i>code@codingRationale</i> • <i>code@validTimeLow</i> • <i>code@validTimeHigh</i> • <i>code@controlInformationRoot</i> • <i>code@controlInformationExtension</i> • <i>code@nullFlavor</i> • <i>code@flavorId</i> • <i>code@updateMode</i>

1088

8.2.8.3 Terminology



All terminology will be provided as generic code files or in a spreadsheet for Step 2.¹⁹

1089

8.2.8.4 Excluded Elements

1090

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

1091

8.2.9 XML SAMPLES: Context of Use

1092

8.2.9.1 Context of Use Elements / Context of Use Keywords

1093

The following is an example of the XML for the Context of Use. The *contextOfUse* enters as a *component* of the *submissionUnit* element. Each component is required to include on priority number element.

1094

1096

```
<component>
```

1097

```
  <priorityNumber value="1000"/>
```

1098

```
  <contextOfUse>
```

1099

```
    <id root="1f080afd-f5d4-4cec-8d09-2bf0ea6bec66"/>
```

1100

```
    <code code="ich 3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
```

1101

```
    <statusCode code="active"/>
```

1102

```
    ...
```

¹⁹ Final Implementation Terminology will be provided on the ESTRi website.

1103 [Additional information may appear after the addition of the *contextOfUse* –
 1104 *primaryInformationRecipient*]
 1105 ...
 1106 <replacementOf typeCode=“RPLC”>
 1107 <relatedContextOfUse>
 1108 <id root=“25fdfdbcb-a2a2-4f2b-a2aa-9ccb4c096acb”/>
 1109 </relatedContextOfUse>
 1110 </replacementOf >
 1111 <derivedFrom>
 1112 <documentReference>
 1113 <id root=“8dc27e78-41ef-4b8d-960d-2626b743f194”/>
 1114 </documentReference>
 1115 </derivedFrom>
 1116 ...
 1117 [Additional information may appear after the addition of the
 1118 *subjectOf.submissionReference*,]
 1119 ...
 1120 <referencedBy typeCode=“REFR”>
 1121 <keyword>
 1122 <code code=“ich species 4” codeSystem=“2.16.840.1.113883.3.989.2.2.4.1.4”/>
 1123 </keyword>
 1124 </referencedBy>
 1125 </contextOfUse>
 1126 </component>
 1127
 1128



See [XML Color Legend](#) for color usage.

1129 The Context of Use element can be ordered by using the priority number to show the order in which
 1130 the Context of Use elements should be displayed when they have the same *ContextOfUse.code* and
 1131 *keyword*. The XML Sample below depicts an example of how both priority number and keywords
 1132 are used in relation to the Context of Use.

1133 <component>
 1134 <priorityNumber value=“1000”/>
 1135 <contextOfUse>
 1136 <id root=“27c069e1-8fec-4b07-907e-cf691543cf66”/>
 1137 <code code=“ich 3.2.s.2.3” codeSystem=“2.16.840.1.113883.3.989.2.2.4.1.1”/>
 1138 <statusCode code=“active”/>
 1139 <derivedFrom>
 1140 <!--Document titled “Controls for Material YYY”-->
 1141 <documentReference>
 1142 <id root=“26a7e20a-b7b6-4729-adcf-75fb90097d68”/>
 1143 </documentReference>
 1144 </derivedFrom>
 1145 <referencedBy typeCode=“REFR”>
 1146 <keyword>

```

1147         <code code="MANU001" codeSystem="2.16.840.1.113883.X"/>
1148     </keyword>
1149 </referencedBy>
1150 <referencedBy typeCode="REFR">
1151     <keyword>
1152         <code code="SUB001" codeSystem="2.16.840.1.113883.X"/>
1153     </keyword>
1154 </referencedBy>
1155 </contextOfUse>
1156 </component>
1157 <component>
1158 <priorityNumber value="2000"/>
1159 <contextOfUse>
1160     <id root="749e6f91-797b-4aeb-89c6-7cf7b9402c15"/>
1161     <code code="ich 3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1162     <statusCode code="active"/>
1163     <derivedFrom>
1164     <!--Document titled "Analytical Method #234"-->
1165         <documentReference>
1166             <id root="57e00a6f-5425-4c0e-98ad-ca4b2e0befea"/>
1167         </documentReference>
1168     </derivedFrom>
1169 <referencedBy typeCode="REFR">
1170     <keyword>
1171         <code code="MANU001" codeSystem="2.16.840.1.113883.X"/>
1172     </keyword>
1173 </referencedBy>
1174 <referencedBy typeCode="REFR">
1175     <keyword>
1176         <code code="SUB001" codeSystem="2.16.840.1.113883.X"/>
1177     </keyword>
1178 </referencedBy>
1179 </contextOfUse>
1180 </component>

```

1181 8.2.9.2 Managing Context of Use Elements

1182 The life cycle management of a *contextOfUse* is covered in this section. Once a *contextOfUse* is
1183 submitted with its id it starts the life cycle for that *contextOfUse*. The following rules have been
1184 harmonized:

- 1185 • When replacing a Context of Use, the two instances must have the same *contextOfUse.code*
1186 and associated Keywords (i.e., this will allow it to appear in exactly the same table of contents
1187 location when it is replaced).
- 1188 • The replacement of Context of Use will make the previous *contextOfUse* element obsolete
1189 (i.e., the *relatedContextOfUse* element(s)).

1190 The following are reasons for changes to the *contextOfUse*:

- 1191 • **New Version:** To version a *contextOfUse*, a different document will need to be indicated in
1192 the *documentReference* element.
- 1193 • **Removal (Suspend) of Context of Use:** If the Context of Use needs to be removed at any
1194 time during the life cycle of the submission, a submission unit may indicate the removal of the
1195 Context of Use by changing the *statusCode* element.
- 1196 • **New Keyword(s):** A Context of Use that needs changes to the keywords would use the
1197 suspension of a CoU and submission of a new CoU.

1198 **8.2.9.2.1 Inserting New Context of Use Elements**

1199 If a *submissionUnit* includes components with the same *contextOfUse* code and *keyword* code, a
1200 priority should be set on the *component* to specify the relative display position of the *contextOfUse*
1201 relative to the other *contextOfUse* elements.

```
1202 <component>
1203 <priorityNumber value="1000"/>
1204   <contextOfUse>
1205     <id root="fd28ce84-651a-437f-b7f0-5171ad21057d"/>
1206     <code code="ich 3.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1207     <statusCode code="active"/>
1208     <derivedFrom>
1209       <!-- Literature Reference Document #1-->
1210       <documentReference>
1211         <id root="0ac0295e-766f-4567-9d63-40b8180de0c0"/>
1212       </documentReference>
1213     </derivedFrom>
1214   </contextOfUse>
1215 </component>
1216 <component>
1217 <priorityNumber value="2000"/>
1218   <contextOfUse>
1219     <id root="d27a4269-eebc-449f-9f33-645907f964984"/>
1220     <code code="ich 3.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1221     <statusCode code="active"/>
1222     <derivedFrom>
1223       <!-- Literature Reference Document #2-->
1224       <documentReference>
1225         <id root="839235d5-1409-46c6-a144-e4fc3988e313"/>
1226       </documentReference>
1227     </derivedFrom>
1228   </contextOfUse>
1229 </component>
```

1230 In subsequent submission units of a submission (i.e., regulatory activity) or application, it may be
1231 necessary to add a Context of Use with the same *contextOfUse.code* as a previous sequence.

1232 The following example adds a new Context of Use with the same *contextOfUse.code* and keywords
1233 as in the previous examples. This Context of Use will appear between the two previously provided
1234 Context of Use elements.

1235 **Inserting Context of Use**

```
1236 <component>
1237 <priorityNumber value="1500"/>
1238   <contextOfUse>
1239     <id root="d5528cfc-15f8-479e-ab59-562c0aa3a5d8"/>
1240     <code code="ich 3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1241     <statusCode code="active"/>
1242     <derivedFrom>
1243       <!--Literature Reference Document #3-->
1244       <documentReference>
1245         <id root="1982f2bf-bd82-45c6-83d7-8838598c971f"/>
1246       </documentReference>
1247     </derivedFrom>
1248   </contextOfUse>
1249 </component>
```

1250 **8.2.9.2.2 Reordering Context of Use**

1251 There will be times when the *contextOfUse* elements may be sent in the incorrect order for display
1252 and the sender wants to correct the order.

1253 Reordering may also need to occur when a new Context of Use needs to be inserted between existing
1254 CoU (see Section 8.2.9.2.2 for additional information). When the *contextOfUse* elements need to be
1255 reordered, the following basic rules should be followed:

- 1256 • If a new component is added during the reordering, that *contextOfUse* element does not use
1257 the *contextOfUse.priorityNumber@updateMode* attribute.
- 1258 • The *contextOfUse.priorityNumber@updateMode* is used for the component being
1259 renumbered

1260 The following example is the basic reordering of the previous context of use that was sent in the
1261 incorrect order. Note: the sender should never or rarely send a submission unit just to reorder
1262 *contextOfUse* elements. The previous Context of Use with a priority number of 1000 does not need
1263 to be sent again in this submission unit.

1264 The following example shows the reordering of a previously submitted Context of Use (note that only
1265 the required elements and attributes are sent) to have a placement prior to the Context of Use with
1266 priority number of 1000.

1267 **Reordering a Context of Use**

```
1268 <component>
1269 <priorityNumber value="900" updateMode="R"/>
1270   <contextOfUse>
1271     <id root="d5528cfc-15f8-479e-ab59-562c0aa3a5d8"/>
1272     <statusCode code="active"/>
```

1273 </contextOfUse>
1274 </component>

1275
1276 Note: the example above does not address the keywords that may be applied to the Context of Use.
1277 For the purposes of the example above, the assumption shows that the Context of Use does not
1278 include keywords.

1279 **8.2.9.2.3 Removing / Suspending Context of Use Elements**

1280 In subsequent submission units, it may be necessary to remove an existing Context of Use (i.e., it is
1281 not being replaced by another Context of Use). In this case, the Context of Use will no longer be
1282 displayed as active.

1283 **Removing a Context of Use**

```
1284 <component>  
1285 <priorityNumber value="900"/>  
1286 <contextOfUse>  
1287 <id root="d5528cfc-15f8-479e-ab59-562c0aa3a5d8"/>  
1288 <statusCode code="suspended"/>  
1289 </contextOfUse>  
1290 </component>
```

1291 **8.2.9.2.4 Replacing (Versioning) Context of Use Elements**

1292 In subsequent submission units of a submission (i.e., regulatory activity), it may be necessary to
1293 replace a *contextOfUse* element within a new *contextOfUse* element. There are two reasons for
1294 submitting a replacement:

- 1295 1. The submission contents (i.e., the document being referenced) have changed
- 1296 2. The previous inactive submission content need to be reinstated as active.

1297 The new *contextOfUse* element will have a new unique identifier and all of the corresponding
1298 attributes. In addition, a *relatedContextOfUse* element is used to identify the Context of Use being
1299 replaced. This is a simple relationship and does not include anything but a reference of the unique
1300 identifier of the *relatedContextOfUse*. The *priorityNumber* of the element should be used to place
1301 content in the correct order based on the desired placement among previously submitted submission
1302 content.

```
1303 <component >  
1304 <priorityNumber value="1000"/>  
1305 <contextOfUse>  
1306 <id root="b205bb7c-a222-4557-a954-0363dc122ca8"/>  
1307 <code code="ich 2.7.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1" />  
1308 <statusCode code="active"/>  
1309 <replacementOf typeCode="RPLC">  
1310 <relatedContextOfUse>  
1311 <id root="78b2f721-25f0-474d-914b-5efb026cc7f7"/>  
1312 </relatedContextOfUse>  
1313 </replacementOf>
```



```

1314     <derivedFrom>
1315     <!--Document-->
1316         <documentReference>
1317             <id root="6ee97feb-8cd1-4991-8c38-002f16102fca"/>
1318         </documentReference>
1319     </derivedFrom>
1320 </contextOfUse>
1321 </component>

```

1322 8.2.10 Application

1323 The Application element is presented in this section of the Implementation Guide as it is the
 1324 connection point for the *document* and *keywordDefinition* elements in the XML message. The
 1325 concept of Application element differs among regions.



Note: Application is primarily a Module 1 concept that will also be described in the Regional/Module 1 Implementation Guide.

1326 8.2.10.1 Location in XML

1327 The *application* element in the XML message is in the following location for documents:

- 1328 • *controlActProcess*>> *subject*>> *submissionUnit*>>*componentOf*>>*submission*>>
 1329 *componentOf*>>*application*

1330 Refer to Table 5: XML Structure for the XML representation.

1331 8.2.10.2 XML Elements

1332 The following is an example of the XML for the application information. The application enters as a
 1333 *componentOf* element between *submission* and *application*.

```

1334 ...
1335 [This XML section will repeat for each application element. A submission element is a componentOf an
1336 application element]
1337 ...
1338 <componentOf>
1339     <application>
1340         <id>
1341             <item root="f23c558f-cd58-41bc-bf6f-c6d230d3d665" extension="987654"/>
1342         ...
1343         <!--Additional item elements can be added here-->
1344         ...
1345         </id>
1346         <code code="C72899" codeSystem="2.16.840.1.113883.3.26.1.1"/>
1347         ...
1348         [Additional information may appear after the addition of the application.code, for
1349         example any of the following elements related to application – component,
1350         referencedBy, informationRecipient, reference, subject, or holder]
1351         ...
1352     </application>
1353 </componentOf>

```

1354



See [XML Color Legend](#) for color usage

1355 The following tables provide a complete set of XML elements and attributes required for the
 1356 **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.

1357 **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..*]		This is the container element of the following attributes by which it uniquely identifies the application, because an application can be given multiple identifiers across territories, one id.item element should be used for each unique application identifier.
	root	[1..1]	Valid UUID	The root attribute of the id element provides a global unique identifier.
	extension	[0..1]	Alpha Numeric <i>e.g., 123456 (U.S. NDA value)</i>	The extension attribute of the id element provides a location to specify a region-specific application tracking number.
Conformance	The id.item@root attribute is required for the application element.			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Business Rules</i>				<p>The <i>id.item@root</i> attribute should stay the same for an <i>id.item@extension</i> value through the entire life cycle of the regulatory activity.</p> <p>The <i>id.item</i> element may be repeated as many times as necessary to indicate one to many application identifier values. Refer to Regional/Module 1 Implementation Guide for assignment of application number.</p>
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>id.item@identifierName</i> • <i>id.item@scope</i> • <i>id.item@reliability</i> • <i>id.item@displayable</i> • <i>id@validTimeLow</i> • <i>id@validTimeHigh</i> • <i>id@controlInformationRoot</i> • <i>id@controlInformationExtension</i> • <i>id@nullFlavor</i> • <i>id@flavorId</i> • <i>id@updateMode</i>

1358 **8.2.10.2.2 application.code**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is the container element that organizes the coded value for the application.
	<i>code</i>	[1..1]	Alpha Numeric <i>Terminology is specified by the appropriate Regional/Module 1 Implementation Guide.</i>	The <i>code</i> attribute is a unique value that indicates the type of content in the application based on regional controlled vocabulary (e.g., NDA, MAA, Art-8-3, Art-10-1, etc.).

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
	codeSystem	[1..1]	Valid OID	The codeSystem attribute is a unique identifier that indicates the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
Conformance	There must be one and only one code@code attribute specified for an application.			
Business Rules	Refer to Regional/Module 1 Implementation Guide for additional information.			
Excluded Elements and/or Attributes	<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • code.displayName • code.originalText • code.translation • code.source • code@codeSystemName • code@codeSystemVersion • code@valueSet • code@valueSetVersion • code@codingRationale • code@validTimeLow • code@validTimeHigh • code@controlInformationRoot • code@controlInformationExtension • code@nullFlavor • code@flavorId • code@updateMode 			

1359

8.2.10.3 Terminology



All terminology will be provided as generic code files or in a spreadsheet for Step 2.²⁰



Refer to the appropriate Regional/Module 1 Implementation Guide for region-specific information for application type codes.

²⁰ Final Implementation Terminology will be provided on the ESTRi website.

1360 **8.2.10.4 Excluded Elements**

1361 No class elements are excluded for the Application element. Refer to Regional/Module 1
 1362 Implementation Guides for more information.

1363 **8.2.11 Document**

1364 The *document* element is used for the purposes of transmitting the information about each document
 1365 related to an application. Documents (e.g., PDF files) are prepared by the Applicant for review by the
 1366 Regulatory Authority. A document may change over time. One document can be associated with
 1367 multiple *contextOfUse* elements, and may be used in multiple submission units.

1368 The initial transmission of a document and its complete set of document elements/attributes are
 1369 considered the creation of a document. Once the document has been identified to the receiving
 1370 system, it can be referenced by its identifier in future uses of the document.

1371 **8.2.11.1 Location in XML**

1372 The *document* element in the XML message is in the following location for documents:

- 1373 • *controlActProcess>> subject>> submissionUnit>>componentOf>>submission>>*
 1374 *componentOf>>application>> component > document*

1375 There may be *holder*, *subject*, or *reference* element prior to the *component* element.

1376 Refer to Table 5: XML Structure for the XML representation.

1377 **8.2.11.2 XML Elements**

1378 The following tables provide a complete set of XML elements and attributes required for the
 1379 *document* element, and any special instructions.



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

1380 Conditions that apply to the *document* element:

- 1381 • One or more *document* elements may follow the *application* element

1382 **8.2.11.2.1 document.id**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>id</i>		[1..1]		This is the container element for the document identifier.
	<i>root</i>	[1..1]	Valid UUID	This <i>root</i> attribute of the <i>id</i> element is a global unique identifier of the <i>document</i> .
Conformance	The <i>root</i> is a required attribute.			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Business Rules</i>				The <i>id@root</i> should be unique for every <i>document</i> element, i.e., there should not be two documents submitted with the same <i>id@root</i> value.
<i>Excluded Elements and/or Attributes</i>				The following datatype attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>id@extension</i> • <i>id@identifierName</i> • <i>id@scope</i> • <i>id@reliability</i> • <i>id@displayable</i> • <i>id@validTimeLow</i> • <i>id@validTimeHigh</i> • <i>id@controlInformationRoot</i> • <i>id@controlInformationExtension</i> • <i>id@nullFlavor</i> • <i>id@flavorId</i> • <i>id@updateMode</i>

1383 **8.2.11.2.2 document.title**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>title</i>		[1..1]		This is the container for the <i>title</i> element of a document.
	<i>value</i>	[1..1]	Alpha Numeric and/or Japanese characters Sender-specified title <i>e.g., "General Information"</i>	This is the <i>value</i> attribute of the <i>title</i> element provides the title for the document. <i>This is a sender-specified value for each document.</i>
	<i>updateMode</i>	[0..1]	Alpha <i>E.g., R= Replace</i>	The <i>updateMode</i> attribute that is used if updating the <i>document.title</i> element.
<i>Conformance</i>				The <i>title@value</i> attribute is required for all documents.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Business Rules</i>				<p>The title element should be used to indicate a human-readable value when displaying the document file.</p> <p>When sending a change in the title element, the title@updateMode attribute should be provided with only a value of “R”. The updateMode should not be used unless an existing Document title is being changed – i.e., avoid using updateMode if the title value is the same.</p> <p>Refer to Section 8.2.15.2 for information about updating document.title.</p>
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • title.translation • title@validTimeLow • title@validTimeHigh • title@controlInformationRoot • title@controlInformationExtension • title@nullFlavor • title@flavorId • title@language

1384 **8.2.11.2.3 document.text**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
text		[0..1]		This is the container element that provides additional information about the document.
	integrityCheckAlgorithm	[1..1]	Alpha Numeric <i>e.g., SHA256</i>	This is the type of integrityCheckAlgorithm that was used for the checksum values provided in integrityCheck element.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
	<i>language</i>	[0..1]	Alpha <i>Refer to ISO 639.1 for two-letter language codes</i> <i>Refer to Regional/Module 1 Implementation Guide</i>	This is the <i>language</i> attribute to indicate the language for the document.
	<i>mediaType</i>	[0..1]	Alpha Numeric <i>Refer to Regional/Module 1 Implementation Guide</i>	This is the <i>mediaType</i> attribute that specifies the usage of the file where it is regionally requested.
<i>text.reference</i>		[0..1]		This is the container element within the <i>text</i> element for a document.
	<i>value</i>	[1..1]	Alpha Numeric File path of the document <i>e.g., “./m3/32-body-data/32s-drug-sub/32s1-gen-info.pdf”</i>	This is the <i>value</i> attribute of the <i>text</i> element that provides the location of the document with the relative path and filename of the document.
<i>text.integrityCheck</i>		[1..1]	Alpha Numeric <i>e.g., “618102bf07065bc1250594201fe448515f0fa61”</i>	This is the integrity check element, which has the checksum value.
<i>Conformance</i>	Documents require the following elements/attributes: <ul style="list-style-type: none"> • The <i>text</i> element <ul style="list-style-type: none"> ○ The <i>text@IntegrityCheckAlgorithm</i> attribute ○ The <i>reference@value</i> attribute ○ The <i>text.integrityCheck</i> element 			

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Business Rules</i>				<p>The <i>text</i> element should be used when sending a document.</p> <p>The <i>text@language</i> and <i>text@mediaType</i> attributes are optional. Refer to Regional/Module 1 Implementation Guides for additional information.</p> <p>For file reuse, the <i>text</i> element must indicate the same <i>reference@value</i>, <i>text@IntegrityCheckAlgorithm</i> and <i>text.integrityCheck</i> values of the previously submitted <i>document</i> element.</p>
<i>Excluded Elements and/or Attributes</i>				<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>text.xml</i> • <i>text.data</i> • <i>text.description</i> • <i>text.thumbnail</i> • <i>text.translation</i> • <i>text@charset</i> • <i>text@compressiontext@translation</i> • <i>text@validTimeLow</i> • <i>text@validTimeHigh</i> • <i>text@controlInformationRoot</i> • <i>text@controlInformationExtension</i> • <i>text@nullFlavor</i> • <i>text@flavorId</i>

1385 **8.2.11.3 Terminology**



There is no controlled terminology for this element.

1386 **8.2.11.4 Excluded Elements**

1387 No class elements are excluded for the *document* element.

1388 **8.2.12 Document Keyword**

1389 All Keywords are applied to the Context of Use – i.e., eCTD v4.0 does not allow document
1390 keywords.

1391 **8.2.13 XML SAMPLES: Application/Document**

1392 The following XML Samples build the *document* element as specified for an Application.

1393 **8.2.13.1 Documents**

1394 The following is an example of a document.

1395 `<document>`
1396 `<id root="973d9293-77b9-4f45-b62e-aae62d7ce814"/>`

```

1397     <title value="Process and Controls"/>
1398     <text integrityCheckAlgorithm="SHA256">
1399         <reference value="../m3/32-prod/manuf-process-and-controls.pdf"/>
1400         <integrityCheck>c0d5623550c997a70b62717d95fca1cada201754d1ed9fbbbbfa97bfd64c8ea4
1401     </integrityCheck>
1402     </text>
1403 </document>

```

1404 **8.2.14 Approaches to Changes in Document Groups**

1405 This section describes the management of *ContextOfUse* elements as document groups consisting of
1406 one or more context of use elements that change over time. The following section provides
1407 information about using keywords to group one or more Context elements together as well as changes
1408 in content composition – i.e., a group of documents may change from one Context of Use to many
1409 Context of Use elements; and many to one.

1410 **8.2.14.1 Use of Keywords for Group Title**

1411 The submitter may use a keyword to add a group title to the Context of Use to further organize
1412 content under a table of contents heading.

```

1413     <component>
1414     <priorityNumber value="1000"/>
1415     <contextOfUse>
1416         <id root="1f271446-8d56-4ddc-b730-eaee208c7053"/>
1417         <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1418         <statusCode code="active"/>
1419         <!--Document Referenced is Analytical Procedure 1-->
1420         <derivedFrom>
1421             <documentReference>
1422                 <id root="164af1e4-f625-4621-8d69-ca56b8f7dc7b"/>
1423             </documentReference>
1424         </derivedFrom>
1425         <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1426 Pack"-->
1427         <referencedBy typeCode="REFR">
1428             <keyword>
1429                 <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1430             </keyword>
1431         </referencedBy>
1432         <!--GT001 is the code for the Group Title Keyword Definition "Analytical
1433 Procedures"-->
1434         <referencedBy typeCode="REFR">
1435             <keyword>
1436                 <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1437             </keyword>
1438         </referencedBy>
1439     </contextOfUse>
1440 </component>
1441 </component>

```

```

1442 <priorityNumber value="2000"/>
1443 <contextOfUse>
1444 <id root="4a5c97e1-4448-47e2-90ff-2d6a264167c0"/>
1445 <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1446 <statusCode code="active"/>
1447 <!--Document Referenced is Analytical Procedure 2-->
1448 <derivedFrom>
1449 <documentReference>
1450 <id root="0127b8b6-5510-45c5-93fd-9a3a6e9735aa"/>
1451 </documentReference>
1452 </derivedFrom>
1453 <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1454 Pack"-->
1455 <referencedBy typeCode="REFR">
1456 <keyword>
1457 <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1458 </keyword>
1459 </referencedBy>
1460 <!--GT001 is the code for the Group Title Keyword Definition "Analytical
1461 Procedures"-->
1462 <referencedBy typeCode="REFR">
1463 <keyword>
1464 <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1465 </keyword>
1466 </referencedBy>
1467 </contextOfUse>
1468 </component>

```

8.2.14.2 One File to Many

1470 This scenario describes a change in content composition where one file (i.e., document) is being
1471 replaced with content being provided by many documents.

1472 Sequence 1

1473 In the first submission unit, the following Context of Use is provided to show a document reference
1474 by a Context of Use.

```

1475 <component>
1476 <priorityNumber value="1000"/>
1477 <contextOfUse>
1478 <id root="1f271446-8d56-4ddc-b730-eaee208c7053"/>
1479 <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1480 <statusCode code="active"/>
1481 <!--Document Referenced is Analytical Procedure 1-->
1482 <derivedFrom>
1483 <documentReference>
1484 <id root="164af1e4-f625-4621-8d69-ca56b8f7dc7b"/>
1485 </documentReference>
1486 </derivedFrom>
1487

```

1488 <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1489 Pack"-->
1490 <referencedBy typeCode="REFR">
1491 <keyword>
1492 <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1493 </keyword>
1494 </referencedBy>
1495 <!--GT001 is the code for the Group Title Keyword Definition "Analytical
1496 Procedures"-->
1497 <referencedBy typeCode="REFR">
1498 <keyword>
1499 <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1500 </keyword>
1501 </referencedBy>
1502 </contextOfUse>
1503 </component>
1504

Sequence 2

The following sample depicts the replacement of the previous Context of Use with two new CoU elements each referencing a document. The Related Context of Use is a reference back to the identifier of the previous Context of Use.

1509 <component>
1510 <priorityNumber value="2000"/>
1511 <contextOfUse>
1512 <id root="0c0abab8-cbfa-4d2f-9793-2b30ea51b8f5"/>
1513 <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1514 <statusCode code="active"/>
1515 <replacementOf typeCode="RPLC">
1516 <relatedContextOfUse>
1517 <id root="1f271446-8d56-4ddc-b730-eaee208c7053" />
1518 </relatedContextOfUse>
1519 </replacementOf>
1520 <!--Document Referenced is Analytical Procedure 1-->
1521 <derivedFrom>
1522 <documentReference>
1523 <id root="164af1e4-f625-4621-8d69-ca56b8f7dc7b"/>
1524 </documentReference>
1525 </derivedFrom>
1526 <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1527 Pack"-->
1528 <referencedBy typeCode="REFR">
1529 <keyword>
1530 <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1531 </keyword>
1532 </referencedBy>
1533 <!--GT001 is the code for the Group Title Keyword Definition "Analytic
1534 Procedures"-->
1535 <referencedBy typeCode="REFR">

```

1536         <keyword>
1537             <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1538         </keyword>
1539     </referencedBy>
1540 </contextOfUse>
1541 </component>
1542 <component>
1543     <priorityNumber value="3000"/>
1544     <contextOfUse>
1545         <id root="4a5c97e1-4448-47e2-90ff-2d6a264167c0"/>
1546         <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1547         <statusCode code="active"/>
1548         <replacementOf typeCode="RPLC">
1549             <relatedContextOfUse>
1550                 <id root="1f271446-8d56-4ddc-b730-eaee208c7053"/>
1551             </relatedContextOfUse>
1552         </replacementOf>
1553         <!--Document Referenced is Analytical Procedure 2-->
1554         <derivedFrom>
1555             <documentReference>
1556                 <id root="0127b8b6-5510-45c5-93fd-9a3a6e9735aa"/>
1557             </documentReference>
1558         </derivedFrom>
1559         <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1560 Pack"-->
1561         <referencedBy typeCode="REFR">
1562             <keyword>
1563                 <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1564             </keyword>
1565         </referencedBy>
1566         <!--GT001 is the code for the Group Title Keyword Definition "Analytic
1567 Procedures"-->
1568         <referencedBy typeCode="REFR">
1569             <keyword>
1570                 <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1571             </keyword>
1572         </referencedBy>
1573     </contextOfUse>
1574 </component>

```

1575 8.2.14.3 Many Files to One

1576 This scenario describes the situations where content provided across multiple files is being replaced
1577 by content provided as a single file. If the initial sequence sent many Context of Use elements (and
1578 thus multiple documents), a subsequent sequence that wants to reference one file would do so by
1579 merging the content into one physical file.

1580 Sequence 1 – Many Documents Referenced

1581 The following sample depicts two *contextOfUse* elements, each referencing a document.

```

1582     <component>
1583         <priorityNumber value="1000"/>
1584         <contextOfUse>
1585             <id root="0c0abab8-cbfa-4d2f-9793-2b30ea51b8f5"/>
1586             <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1587             <statusCode code="active"/>
1588             <!--Document Referenced is Analytical Procedure 1-->
1589             <derivedFrom>
1590                 <documentReference>
1591                     <id root="164af1e4-f625-4621-8d69-ca56b8f7dc7b"/>
1592                 </documentReference>
1593             </derivedFrom>
1594             <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1595 Pack"-->
1596             <referencedBy typeCode="REFR">
1597                 <keyword>
1598                     <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1599                 </keyword>
1600             </referencedBy>
1601             <!--GT001 is the code for the Group Title Keyword Definition "Analytical
1602 Procedures"-->
1603             <referencedBy typeCode="REFR">
1604                 <keyword>
1605                     <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1606                 </keyword>
1607             </referencedBy>
1608         </contextOfUse>
1609     </component>
1610     <component>
1611         <priorityNumber value="2000"/>
1612         <contextOfUse>
1613             <id root="4a5c97e1-4448-47e2-90ff-2d6a264167c0"/>
1614             <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1615             <statusCode code="active"/>
1616             <!--Document Referenced is Analytical Procedure 2-->
1617             <derivedFrom>
1618                 <documentReference>
1619                     <id root="0127b8b6-5510-45c5-93fd-9a3a6e9735aa"/>
1620                 </documentReference>
1621             </derivedFrom>
1622             <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1623 Pack"-->
1624             <referencedBy typeCode="REFR">
1625                 <keyword>
1626                     <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1627                 </keyword>
1628             </referencedBy>

```

```

1629           <!--GT001 is the code for the Group Title Keyword Definition "Analytical
1630 Procedures"-->
1631           <referencedBy typeCode="REFR">
1632             <keyword>
1633               <code code="GT00" codeSystem="2.16.840.1.113883.3"/>
1634             </keyword>
1635           </referencedBy>
1636         </contextOfUse>
1637       </component>
1638

```

Sequence 2 – One Document Referenced

The following sample shows that the three previous Context of Use elements are replaced by one Context of Use referencing a document (the document now contains all of the content previously submitted in three separate documents).

```

1644       <component>
1645         <priorityNumber value="1100"/>
1646         <contextOfUse>
1647           <id root="49e18e35-fe1b-4929-bf30-ea58c81ec30f"/>
1648           <code code="ich 3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1649           <statusCode code="active"/>
1650           <replacementOf typeCode="RPLC">
1651             <relatedContextOfUse>
1652               <id root="0c0abab8-cbfa-4d2f-9793-2b30ea51b8f5"/>
1653             </relatedContextOfUse>
1654           </replacementOf>
1655           <replacementOf typeCode="RPLC">
1656             <relatedContextOfUse>
1657               <id root="4a5c97e1-4448-47e2-90ff-2d6a264167c0"/>
1658             </relatedContextOfUse>
1659           </replacementOf>
1660           <!--Document Referenced is Analytical Procedure Consolidated-->
1661           <derivedFrom>
1662             <documentReference>
1663               <id root="e8e44446-de99-4324-ba9c-502fe8d729ba"/>
1664             </documentReference>
1665           </derivedFrom>
1666           <!--C001 is the code for the Group Title Keyword Definition "PVDC Blister
1667 Pack"-->
1668           <referencedBy typeCode="REFR">
1669             <keyword>
1670               <code code="C001" codeSystem="2.16.840.1.113883.3"/>
1671             </keyword>
1672           </referencedBy>
1673           <!--GT001 is the code for the Group Title Keyword Definition "Analytical
1674 Procedures"-->
1675           <referencedBy typeCode="REFR">
1676             <keyword>

```

```

1677         <code code="GT001" codeSystem="2.16.840.1.113883.3"/>
1678     </keyword>
1679 </referencedBy>
1680 </contextOfUse>
1681 </component>

```

1682 8.2.15 Other Considerations

1683 8.2.15.1 Document Reuse

1684 A Document can be referenced many times in the life cycle of the application. Therefore, the reuse of
1685 documents is an important feature of eCTD v4.0. Reuse of documents can be used when the
1686 document accurately represents the content and metadata that should be present under another
1687 Context of Use. The most common examples of document reuse will be depicted in this section.

1688 Refer to Regional/Module 1 Implementation Guides for additional information on document retention
1689 practices and rules for Document Reuse.

1690
1691
1692 When the same document is being sent within or across submission units, the *document* element only
1693 needs to be provided once to establish the document identifier, which can then be referenced by any
1694 reference in a Context of Use element.

1695 Below, the XML shows two Context of Use elements that reference the same document by its
1696 document identifier.

1697 Sequence 1

1698 *Context of Use Element*

```

1699 <component>
1700 <priorityNumber value="1000"/>
1701 <contextOfUse>
1702     <id root="7480bc1a-6486-4714-8d32-a3bd41de9be6"/>
1703     <code code="ich 3.2.a.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1" />
1704     <statusCode code="active"/>
1705     <derivedFrom>
1706         <documentReference>
1707             <id root="3d1084fb-56c6-4923-a1e5-8a15e4fdc9c5"/>
1708         </documentReference>
1709     </derivedFrom>
1710 </contextOfUse>
1711 </component>

```

Document.id
provided in
Sequence 1

1713 *Document element*

```

1714 <document>
1715     <id root="3d1084fb-56c6-4923-a1e5-8a15e4fdc9c5"/>
1716     <title value="Excipients X"/>
1717     <text integrityCheckAlgorithm="SHA256">
1718         <reference value="../../../m3/32-prod/excipients.pdf"/>
1719         <integrityCheck>c0d5623550c997a70b62717d95fca1cada201754d1ed9fbbbf97bfd64c8ea4
1720     </integrityCheck>

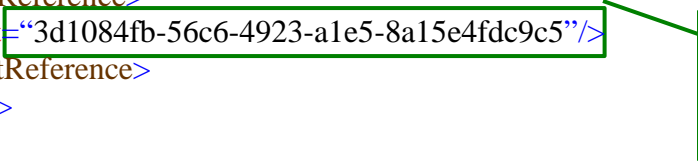
```

Document.id


```

1721     </text>
1722 </document>
1723
1724 Sequence 2
1725
1726 Context of Use Element
1727 <component>
1728 <priorityNumber value="2000"/>
1729   <contextOfUse>
1730     <id root="47939431-1ac1-4e17-b44d-dcea7ce43050"/>
1731     <code code="ich 3.2.a.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1" />
1732     <statusCode code="active"/>
1733     <derivedFrom>
1734       <documentReference>
1735         <id root="3d1084fb-56c6-4923-a1e5-8a15e4fdc9c5"/>
1736       </documentReference>
1737     </derivedFrom>
1738   </contextOfUse>
1739 </component>

```



Document.id
provided in
Sequence 1

1741 *Document Element*

1742 The **document** element is not sent in this submission unit. The document was sent in the previous
 1743 sequence 1.

1744 **8.2.15.2 Document Title Updates**

1745 If the sender has sent a **document** element with an error in the **document.title** element, it can be
 1746 updated without creating an entirely new document. The example provided in this section, will
 1747 indicate the required elements for such an update.

1748 **Initial submission of document**

```

1749 <document>
1750   <id root="ceb05f3d-ebb0-4547-9734-056efa134a7a"/>
1751   <title value="Process and Controls"/>
1752   <text integrityCheckAlgorithm="SHA256">
1753     <reference value="../m3/32-prod/manuf-process-and-controls.pdf"/>
1754     <integrityCheck>a4c828974a7d177137d69aedfc45379a694611ef317c6c1741a935aa9555c57
1755   d</integrityCheck>
1756   </text>
1757 </document>

```

1759 **Update to Document Title using updateMode**

```

1760 <document>
1761   <id root="ceb05f3d-ebb0-4547-9734-056efa134a7a"/>
1762   <title value="Manufacturing Process and Controls" updateMode="R"/>
1763 </document>

```

1764 8.2.15.3 File Reuse

1765 A file is usually represented by one *document* element and that *document* element can be referenced
1766 by multiple *ContextofUse* elements. This is described in the Document Reuse section. In certain
1767 situations, a file may need to be presented differently in one usage versus another (e.g., different
1768 document title). In these rare situations the file would need to be represented by an additional
1769 *document* element. Thus the same file path may appear in multiple *document.text* elements. The file
1770 only needs to be sent once in the folder structure. This is described in the Document Reuse section
1771 (See section 8.2.15.1).

1772 Files can be reused across submissions and applications (see note below) by providing the file path of
1773 a previously submitted file when defining a new *document* element for that submission or
1774 application. The file will be retrieved from its original folder location.

1775 Note: if files are reused, i.e., sent once in the original folder structure, the manual navigation of the
1776 folder structure will become more difficult as all files within a submission unit, submission or
1777 application may not be contained in the same physical folder location.

1778 Note: Refer to Regional/Module 1 Implementation Guides for region-specific information about file
1779 reuse.

1780 The following XML sample describes a *document* element with the title "Report for Study 1" and a
1781 document code identifying it as a study report body.

```
1782 <component>  
1783   <document>  
1784     <id root="bab246ef-7d8e-4042-bd8b-ad9769f4589b"/>  
1785     <title value="Report for Study 1"/>  
1786     <text integrityCheckAlgorithm="SHA256" language="en">  
1787       <reference value="../m5/531-biopharm/report1.pdf"/>  
1788       <integrityCheck>5b94eb14cd31031a4d4539d0bcfbef028a91c04d2d2575990c4422947a9f  
1789       437a</integrityCheck>  
1790     </text>  
1791   </document>  
1792 </component>
```

1794 The following *document* element describes the same file from the previous example with a slightly
1795 different document title. This *document* element is being created in a subsequent submission unit
1796 from the original submission of the file; notice the difference in the file path information provided in
1797 these examples.

```
1798 <component>  
1799   <document>  
1800     <id root="79da2f37-02a8-4dcd-8552-54565b093c08"/>  
1801     <title value="Summary Report for Study 1"/>  
1802     <text integrityCheckAlgorithm="SHA256" language="en">  
1803       <reference value="../second-level-folder/m5/531-biopharm/report1.pdf"/>  
1804       <integrityCheck>  
1805 5b94eb14cd31031a4d4539d0bcfbef028a91c04d2d2575990c4422947a9f437a </integrityCheck>  
1806     </text>
```

1807 </document>

1808 </component>

1809 **8.2.16 Keyword Definition**

1810 The *keywordDefinition* is used to define a sender-specified keyword that will be referenced by a code
1811 in other parts of the message. The use of keyword definitions is mainly for defining keyword values
1812 that are not defined by a controlled vocabulary (e.g., sender-specific keywords). A keyword
1813 definition contains name value pairs that are used to provide Keywords on the Context of Use.

1814 **8.2.16.1 Location in XML**

1815 The *keywordDefinition* element in the XML message is in the following location for keyword
1816 definitions:

- 1817 • *controlActProcess*>> *subject*>> *submissionUnit*>>*componentOf*>>*submission*>>
1818 *componentOf*>>*application*>> *referencedBy*> *keywordDefinition*

1819 There may be *informationRecipient*, *holder*, *reference* or *subject* elements prior to the *referencedBy*
1820 element.

1821 Refer to Table 5: XML Structure for the XML representation.

1822 **8.2.16.2 XML Elements**

1823 The following tables provide a complete set of XML elements and attributes required for the
1824 *keywordDefinition* 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.

1825 Each *keywordDefinition* should be sent in its own *keywordDefinition* element. Although the schema
1826 allows multiple values for each *keywordDefinition*, the eCTD v4.0 only allows one item per
1827 *keywordDefinition* element.

1828

1829 Conditions that apply to the *keywordDefinition* element:

- 1830 • Zero to many *keywordDefinition* elements can be sent for each *application* element
- 1831 • A *keywordDefinition* should be provided for sender-specified keywords.
- 1832 • The *keywordDefinition* only needs to be provided once for an Application – i.e., the keyword
1833 definition should be defined once and referenced by its assigned code value. Note: the
1834 *keywordDefinition* will need to be defined for each new Application.

1835

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is the container element that identifies the type of keyword definition.
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., “ich-manufacturer”</i>	This is the <i>code</i> attribute for the coded value of the type of keyword definition.
	<i>codeSystem</i>	[1..1]	Valid OID	This is the <i>codeSystem</i> OID that is a unique identifier for the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
<i>Conformance</i>	The <i>code</i> and <i>codeSystem</i> are required attributes.			
<i>Business Rules</i>	The <i>code</i> must be from a valid ICH Keyword code type.			
<i>Excluded Elements and/or Attributes</i>	The following datatype elements and attributes may not be required by eCTD v4.0: <ul style="list-style-type: none"> • <i>code.displayName</i> • <i>code.originalText</i> • <i>code.translation</i> • <i>code.source</i> • <i>code@codeSystemName</i> • <i>code@codeSystemVersion</i> • <i>code@valueSet</i> • <i>code@valueSetVersion</i> • <i>code@codingRationale</i> • <i>code@validTimeLow</i> • <i>code@validTimeHigh</i> • <i>code@controlInformationRoot</i> • <i>code@controlInformationExtension</i> • <i>code@nullFlavor</i> • <i>code@flavorId</i> • <i>code@updateMode</i> 			

1838 **8.2.16.2.2** *keywordDefinition.statusCode*

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>statusCode</i>		[1..1]		This is the container element that identifies the status of the <i>keywordDefinition</i> .
	<i>code</i>	[1..1]	Alpha e.g., <i>active</i>	This is the code value for the status.
<i>Conformance</i>	The <i>statusCode</i> is required.			
<i>Business Rules</i>	The <i>code</i> attribute should always have a value of “active”.			
<i>Excluded Elements and/or Attributes</i>	<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>statusCode.part</i> • <i>statusCode@validTimeLow</i> • <i>statusCode@validTimeHigh</i> • <i>statusCode@controlInformationRoot</i> • <i>statusCode@controlInformationExtension</i> • <i>statusCode@nullFlavor</i> • <i>statusCode@flavorId</i> • <i>statusCode@updateMode</i> 			

1839 **8.2.16.2.3** *keywordDefinition.value*

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>value</i>		[1..1]		This is the container element for the keyword defined for the keyword code provided for <i>keywordDefinition</i> .
<i>value.item</i>		[1..1]		This is the container element to specify an individual keyword identifier.
	<i>code</i>	[1..1]	Alpha Numeric Sender specified value e.g., <i>MANU001</i>	This is the <i>code</i> attribute for the keyword being defined.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
	<i>codeSystem</i>	[1..1]	Valid OID	This is the <i>codeSystem</i> OID that is a unique identifier for the controlled vocabulary system.
<i>value.item.displayName</i>		[1..1]		This is the container element to specify the <i>displayName</i> , which is the value of the keywordDefinition code.
	<i>value</i>	[1..1]	Alpha Numeric <i>Sender specified value e.g., “Big Manufacturer”</i>	The <i>displayName</i> attribute of the <i>value</i> element of the keyword being defined.
	<i>updateMode</i>	[0..1]	Alpha <i>e.g., R=Replace</i>	The <i>updateMode</i> should be used to make changes to the Keyword Definition’s display name value.
<i>Conformance</i>	<p><i>The keywordDefinition.value</i> is a required element.</p> <p>The <i>value.item@code</i>, <i>value.item@codeSystem</i> and <i>value.item.displayName@value</i> are required attributes.</p>			
<i>Business Rules</i>	<p>Each <i>keywordDefinition</i> can only contain one sender-specified keyword.</p> <p>The <i>displayName@value</i> is the only attribute that can be updated, at which time the <i>displayName@updateMode</i> should only be provided with a value of “R”. The <i>updateMode</i> should not be used unless the <i>displayName@value</i> is being changed – i.e., avoid using update mode if the value is not being updated for the keyword definition.</p>			
<i>Excluded Elements and/or Attributes</i>	<p>The following datatype elements and attributes may not be required by eCTD v4.0:</p> <ul style="list-style-type: none"> • <i>displayName@controlInformationExtension</i> • <i>displayName@controlInformationRoot</i> • <i>displayName@flavorId</i> • <i>displayName@language</i> • <i>displayName@nullFlavor</i> • <i>displayName@validTimeHigh</i> • <i>displayName@validTimeLow</i> 			

1840 **8.2.16.3 Terminology**



All terminology will be provided as generic code files or in a spreadsheet for Step 2.²¹

1841 **8.2.16.4 Excluded Elements**

1842 No class elements are excluded for the *keywordDefinition* element.

1843 **8.2.17 XML SAMPLES: Keyword Definition**

1844 At this time, keywords should only be defined for an application – i.e., keyword definitions should
1845 not be reused across applications. The following sections outline the additional scenarios for XML
1846 instances in defining and using keywords.

1847 **8.2.17.1 Keyword Definitions**

1848 The following XML sample shows one *keywordDefinition* of type, manufacturer.

```
1849  
1850 <referencedBy>  
1851   <keywordDefinition>  
1852     <code code="ich keyword type 3"  
1853       codeSystem="2.16.840.1.113883.3.989.2.2.4.1.2"/>  
1854     <statusCode code="active"/>  
1855     <value>  
1856       <item code="MANU001" codeSystem="CompanyOID-  
1857         ManufacturerKeyword">  
1858         <displayName value="Big Manufacturer"/>  
1859       </item>  
1860     </value>  
1861   </keywordDefinition>  
1862 </referencedBy>
```

1863
1864 Note: that one item value per keyword definition is required; the schema allows for multiple.



See [XML Color Legend](#) for color usage.

1865 **8.2.17.2 Keyword Definition display name change**

1866 Keyword Definitions that are sent may have been sent with errors. If the sender needs to correct the
1867 display name of a keyword definition (i.e., it is the same concept or term with a correct representation
1868 (e.g., spelling)) only the display name may be altered. The keyword definition code shall remain the
1869 same.

1870 **Sequence 1**

```
1871 <referencedBy>  
1872   <keywordDefinition>  
1873     <code code="ich keyword type 3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.2"/>  
1874     <statusCode code="active"/>
```

²¹ Final Implementation Terminology will be provided on the ESTRI website.

```

1875         <value>
1876             <item code="MANU001" codeSystem="CompanyOID-ManufacturerKeyword">
1877                 <displayName value="Ace Manufacturer"/>
1878             </item>
1879         </value>
1880     </keywordDefinition>
1881 </referencedBy>
1882

```

1883 Sequence 2

```

1884 <referencedBy>
1885     <keywordDefinition>
1886         <code code="ich keyword type 3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.2"/>
1887         <statusCode code="active"/>
1888         <value>
1889             <item code="MANU001" codeSystem="CompanyOID-ManufacturerKeyword">
1890                 <displayName value="Acme Manufacturer" updateMode="R"/>
1891             </item>
1892         </value>
1893     </keywordDefinition>
1894 </referencedBy>
1895

```

displayName changed
to correct value.

1896 Note: Refer to Regional/Module 1 Implementation Guides for information on the keyword definition
1897 display name when it needs to be updated in just the referenced submission or for all uses in the
1898 application.

1899 8.2.17.3 Use of Keyword Definitions across Submission Units

1900 Keyword Definitions once they have been sent by the sender do not need to be sent again unless there
1901 is a change to the definition. The keyword code shall stay the same across submission units within an
1902 application – i.e., only the display name can be changed. There should only be one keyword
1903 definition code and display name pair defined for a particular concept – i.e., one concept shall not be
1904 defined more than once within an application.

1905 Sequence 1

1906 Keyword Defined in Sequence 1

```

1907 <referencedBy>
1908     <keywordDefinition>
1909         <code code="ich keyword type 3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.2"/>
1910         <statusCode code="active"/>
1911         <value>
1912             <item code="MANU003" codeSystem="CompanyOID-ManufacturerKeyword">
1913                 <displayName value="Simple Manufacturer"/>
1914             </item>
1915         </value>
1916     </keywordDefinition>
1917 </referencedBy>

```


1918 **Keyword Definition used by Context of Use in Sequence 1**

```
1919 <component>
1920 <priorityNumber value="1000"/>
1921 <contextOfUse>
1922 <id root="8c590801-c4ca-4940-bb4d-5a4cd32685d7"/>
1923 <code code="ich 3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1924 <statusCode code="active"/>
1925 <derivedFrom>
1926 <!--Document titled "Controls for Material YYY"-->
1927 <documentReference>
1928 <id root="d0c6463c-7538-4ac8-827d-65b083c3893d"/>
1929 </documentReference>
1930 </derivedFrom>
1931 <referencedBy typeCode="REFR">
1932 <keyword>
1933 <code code="MANU003" codeSystem="2.16.840.1.113883.X"/>
1934 </keyword>
1935 </referencedBy>
1936 <referencedBy typeCode="REFR">
1937 <keyword>
1938 <code code="SUB001" codeSystem="2.16.840.1.113883.X"/>
1939 </keyword>
1940 </referencedBy>
1941 </contextOfUse>
1942 </component>
1943 Keyword Defined in Sequence 3
```

1944 No additional information sent in the XML for the Keyword Definition. The value sent in sequence
1945 1, "MANU003" with display name "Simple Manufacturer" is still applicable.

1946 **Keyword Definition used by Context of Use in Sequence 3**

```
1947 <component>
1948 <priorityNumber value="2000"/>
1949 <contextOfUse>
1950 <id root="64e51fb8-4608-4c3a-af52-68b5cc02345b"/>
1951 <code code="ich 3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
1952 <statusCode code="active"/>
1953 <derivedFrom>
1954 <!--Document titled "Controls for Material BCD"-->
1955 <documentReference>
1956 <id root="23967c61-99bf-4090-863c-15b524ee242e"/>
1957 </documentReference>
1958 </derivedFrom>
1959 <referencedBy typeCode="REFR">
1960 <keyword>
1961 <code code="MANU003" codeSystem="2.16.840.1.113883.X"/>
1962 </keyword>
```

1963 </referencedBy>
1964 <referencedBy typeCode="REFR">
1965 <keyword>
1966 <code code="SUB001" codeSystem="2.16.840.1.113883.X"/>
1967 </keyword>
1968 </referencedBy>
1969 </contextOfUse>
1970 </component>
1971

1972 **9. DOSSIER MANAGEMENT**

1973 Dossier Management refers to the life cycle management of submission units, submissions (e.g.,
1974 regulatory activities) and applications. Although this topic is very important to eCTD v4.0, it is not
1975 covered in this Implementation Guide. Due to the variation in regulatory processes across regions as
1976 to how to manage the life cycle as well as the precise definition of these concepts in each region, this
1977 information will be found in the Regional/Module 1 Implementation Guides.

1978

1979 **10. COMPATIBILITY AND REFERENCE TO eCTD V3.2.2**

1980 In order to prepare for the transition of a dossier from an eCTD v3.2.2 message to an eCTD v4.0
1981 message, there are several considerations noted below:

- 1982
- 1983 • The transition mapping message should be used for administrative purposes only. Although
1984 the RPS R2 Normative schema is being leveraged for the transition mapping instance, it is not
1985 meant to function as a v4.0 message; and therefore does not follow all of the same rules stated
1986 in the main body of this implementation guide.
 - 1987 • The transition activity shall enable a seamless presentation of information to the
1988 builders/viewers/reviewers i.e., one tool to support viewing of v3.2.2 and v4.0. Although the
1989 transition mapping message will not recreate the presentation of submission content, the data
1990 elements sent forward will be used to enable the following two objectives:
 - 1991 ○ To maintain Context of Use life cycle in new submissions/regulatory activities
 - 1992 ○ To enable the reuse of documents within and across applications
 - 1993 • There is also a desire to have the ability to disconnect completely from v3.2.2 at a point in the
1994 future, so the approach should support the eventual retirement of v3.2.2 – i.e., there will be a
1995 point in time that all applications with activity must be transitioned.
 - 1996 • The Region will determine if the transition mapping message can be executed before or
1997 during a regulatory activity.



Implementers – these instructions should enable a specific transition mapping message, which will have its own instruction, and validation rules. Refer to Regional/Module 1 Implementation Guide for specific details.

1998 **10.1 Overview of Forward Compatibility**

1999 There will be one way to transition from v3.2.2 to v4.0 messages to meet the stated objectives of
2000 forward compatibility. The applicant needs to submit a “Current View” message that will transition
2001 all current content to v4.0 in one message. The forward compatibility transition mapping message
2002 will be based on the Current View, which is defined as follows:

- 2003
- 2004 • Only submission content that has been submitted to the Regulator should be included in the
2005 transition mapping
 - 2006 • All current submission contents* should be transitioned regardless of whether or not the
2007 content will undergo life cycle
 - 2008 • Any sequences under development should be submitted after the transition mapping
2009 submission

2010 * Excludes any leaf elements that were deleted or replaced

2011 Once the applicant submits the forward compatibility transition message the following actions may be
2012 taken:

- 2013
- 2014 • Perform any submission content life cycle thereafter on any of the content in a v4.0 message;
2015 or
 - 2016 • Use of the transition mapping message when selling the product and transferring application
2017 content to the new owner.

2017 **10.2 Schema**

2018 RPS Schema used for transition message and all required elements will be included. Since the
2019 schema does not include additional constraints or machine readable validations, the same schema can
2020 be used for both the transition mapping message as well as the v4.0 message.



Implementers – if any additional constraints or patterns are added to

implementation schemas, there may need to be adjustments to meet the transition mapping requirements.

2021 **10.3 Included Elements**

2022 The transition mapping message will only contain the minimum set of elements and attributes
2023 necessary to complete the transition. The following elements are considered required for the
2024 complete preparation of a v3.2.2 message to a v4.0 message.

- 2025 • SubmissionUnit
 - 2026 ○ Id
 - 2027 ○ Code
 - 2028 • CoU
 - 2029 ○ Priority Number (respective to the CoU Code and Keyword combo)
 - 2030 ○ Id
 - 2031 ○ Code
 - 2032 ○ Status code
 - 2033 ○ Document Reference
 - 2034 ○ Keyword
 - 2035 • Sequence Number
 - 2036 • Submission
 - 2037 • Application
 - 2038 ○ Id
 - 2039 ○ Code
 - 2040 • Document
 - 2041 ○ Id (version 4.0)
 - 2042 ○ Reference value
 - 2043 ○ Leaf reference (URI algorithm -- SequenceNumber.xmltype.leafId (e.g.,
 - 2044 0032.ich#NLAS57D17EB601C9EDCA))
 - 2045 • Keyword Definition
 - 2046 ○ Code – type
 - 2047 ○ Code for keyword value
 - 2048 ○ Status Code
 - 2049 ○ Value for display name
 - 2050 • Contact Party for Technical Contact
 - 2051 ○ Contact Party type
 - 2052 ○ Person identifier
 - 2053 ○ Person name
 - 2054 ○ Person telecom
- 2055
- 2056

2057 **10.3.1 Submission Unit**

2058 The Submission Unit element in the transition mapping message will include the following elements:

- 2059 • *submissionUnit.id*

2060 All other elements typically provided for a submission unit will be ignored if submitted including:

- 2061 • *code*
 2062 • *title*
 2063 • *statusCode*
 2064 • *component1.sequenceNumber*
 2065 • *component2.CategoryEvent*
 2066

2067 These elements are not necessary for the transition mapping submission unit. Only the identifier for
 2068 the administrative filing is required.

2069 **10.3.1.1 XML Elements**

2070 The following tables provide a complete set of XML elements and attributes required for the
 2071 *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.

2072 **10.3.1.1.1 SubmissionUnit.id**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>id</i>		[1..1]		This is the container element that uniquely identifies the submission unit sent in the message.
	<i>root</i>	[1..1]	Valid UUID	This is the <i>root</i> attribute that uniquely identifies the submission unit.
<i>Conformance</i>	The <i>id@root</i> is a required attribute.			
<i>Business Rules</i>	The <i>id@root</i> should be unique for every <i>submissionUnit</i> .			

2073

2074 **10.3.2 Priority Number for Context of Use**

2075 The priority number is required in the transition mapping message. It will be used for future order
 2076 and display purposes.

2077 **10.3.2.1 XML Elements**

2078 The following table provides a complete set of XML elements and attributes required for the
 2079 *component.priorityNumber* element, and any special instructions.



The *typeCode* is not required in the eCTD v4.0 XML message. The *typeCode* is fixed to “COMP”. If the XML message contains any other value for this attribute it will be invalid against the schema.

2080 **10.3.2.1.1 priorityNumber**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>priorityNumber</i>		[1..1]		This is the container element for the priority number and its value.
	<i>value</i>	[1..1]	Numeric <i>e.g., 1000,2000, 3000</i>	The <i>value</i> attribute of the <i>priorityNumber</i> provides a whole number to be used for ordering the Context of Use element.
<i>Conformance</i>		<i>priorityNumber@value</i> attribute is required.		
<i>Business Rules</i>		<p>The priority number is required for each contextOfUse element.</p> <p>The value shall be a positive integer up to 6 digits (i.e., 1 – 999999) for the contextOfUse element with the same Context of Use code value and Keyword code value pair.</p> <p>It is recommended to start with “1000” and intervals of 1000 (e.g., “2000”, “3000”, etc.) for the initial submission of a CoU sharing the same CoU/ keyword code combination. This allows increments of one, tens and hundreds to be used when reordering and/or inserting CoU.</p> <p>The priority number should not be duplicated within the same CoU code and Keyword combinations. Refer to Regional/Module 1 Implementation Guides for additional business rules for priority number conflicts.</p> <p>The priority number will be used to order the Context of Use elements within the same CoU code and keyword combinations when displayed.</p>		

2081 **10.3.3 Context of Use**

2082 The Context of Use is critical in the transition mapping message as it prepares the existing leaf to
 2083 undergo a life cycle operation in future eCTD v4.0 messages.

2084 **10.3.3.1 XML Elements**

2085 The following tables provide a complete set of XML elements and attributes required for the
 2086 *contextOfUse* element, and any special instructions.



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

2087 **10.3.3.1.1 contextOfUse.id**

Element	Attribute	Cardinality	Value(s) Allowed	Description Instructions
<i>id</i>		[1..1]		This is the container element that organizes the <i>contextOfUse</i> identifier.
	<i>root</i>	[1..1]	Valid UUID	The <i>root</i> attribute of the <i>id</i> element provides a global unique identifier of the <i>contextOfUse</i> .
<i>Conformance</i>	<i>id@root</i> is a required attribute.			
<i>Business Rules</i>	The <i>id@root</i> should be unique for every <i>contextOfUse</i> submitted.			

2088 **10.3.3.1.2 contextOfUse.code**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>code</i>		[0..1]		This is the container element for the type of content referenced under the <i>contextOfUse</i> .
	<i>code</i>	[1..1]	Alpha Numeric	The <i>code</i> attribute provides a coded value that indicates the heading and is defined by ICH or Regulatory Authorities.
	<i>codeSystem</i>	[1..1]	Valid OID	The <i>codeSystem</i> attribute provides a unique identifier that indicates the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>Conformance</i>	The <i>code</i> and <i>codeSystem</i> attributes must be provided; and they must match the values of the existing leaf. The code values will be validated during the review of the transition mapping message.			
<i>Business Rules</i>	The <i>code</i> element is required when sending the Context of Use.			

2089 **10.3.3.1.3 contextOfUse.statusCode**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>statusCode</i>		[1..1]		This is the container element that has a controlled terminology code that indicates the status of the Context of Use.
	<i>code</i>	[1..1]	Alpha “active”	The <i>code</i> attribute provides a specified value that indicates whether the Context of Use is still relevant or if it has been removed.
<i>Conformance</i>	The <i>statusCode</i> element is always required and must be “active”.			
<i>Business Rules</i>	The <i>statusCode@code</i> must always be sent in the message.			

2090

2091 **10.3.4 Document Reference**

2092 This element is a reference to a document sent in the current transition mapping message submission
2093 unit or a previously submitted transition mapping message submission unit.

2094 **10.3.4.1 XML Elements**

2095 The following table provides a complete set of XML elements and attributes required for the
2096 *documentReference* element, and any special instructions.



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

2097 **10.3.4.1.1 documentReference.id**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>id</i>		[1..1]		This is the container element for a reference to a Document.
	<i>root</i>	[1..1]	Valid UUID	The <i>root</i> attribute or the <i>id</i> element provides a global unique identifier of the Document being referenced.
<i>Conformance</i>	The <i>id@root</i> attribute is required.			
<i>Business Rules</i>	The <i>id@root</i> is a reference to a document sent in the current transition mapping message submission unit or a previously submitted transition mapping message submission unit.			

2098

2099 **10.3.5 Keyword**

2100 All keywords associated with a v3.2.2 leaf should be added to the Context of Use element as a
 2101 referencedBy association. These keywords may be included in the leaf or as external file-tags. All
 2102 existing values shall be provided regardless of keyword type – i.e., now part of a controlled
 2103 vocabulary or a keyword definition.

2104 **10.3.5.1 XML Elements**

2105 The following tables provide a complete set of XML elements and attributes required for the *keyword*
 2106 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 *typeCode* is required in the eCTD v4.0 XML message. The *typeCode* should be to “REFR”. If the XML message contains any other value for this attribute it will be invalid against the schema.

2107 **10.3.5.1.1 keyword.code**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>code</i>		[1..1]		This is the container element that identifies the keyword.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., “M123456” for Manufactur e Site</i>	This is the <i>code</i> attribute that identifies the code value for the keyword.
	<i>codeSystem</i>	[1..1]	Valid OID	This is the <i>codeSystem</i> OID that is a unique identifier for the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
<i>Conformance</i>	The <i>code</i> and <i>codeSystem</i> attributes are required. A keyword can only have one code.			
<i>Business Rules</i>	The display name for the <i>code</i> needs to be retrieved from the corresponding code system.			

2108 **10.3.6 XML SAMPLE: Transition mapping of Context of Use Elements and**
2109 **Keywords**

2110 The following is an example of the XML for the Context of Use and Keywords for the transition
2111 mapping message.

2112 **Context of Use with Keywords**

```

2113 <component>
2114 <priorityNumber value="1000"/>
2115 <contextOfUse>
2116 <id root="d82eb3db-04ed-48d8-85db-4a83ba1efb6d"/>
2117 <code code="ich3.2.p.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1"/>
2118 <statusCode code="active"/>
2119 <derivedFrom>
2120 <documentReference>
2121 <id root="3452ada4-7f91-49dd-be9d-fee71d0ca3e8"/>
2122 </documentReference>
2123 </derivedFrom>
2124 <referencedBy typeCode="REFR">
2125 <keyword>
2126 <code code="PRD-001" codeSystem="2.16.840.1.113883.3.989"/>
2127 </keyword>
2128 </referencedBy>

```

2129 <referencedBy typeCode="REFR">
 2130 <keyword>
 2131 <code code="DOSE-001" codeSystem="2.16.840.1.113883.3.989"/>
 2132 </keyword>
 2133 </referencedBy>
 2134 </contextOfUse>
 2135 </component>
 2136



See [XML Color Legend](#) for color usage.

2137 **10.3.7 Sequence Number**

2138 The *sequenceNumber* is an increasing numeric value used to maintain a sequential and chronological
 2139 order within the submission or across submissions; and it is unique within an Application.

2140 **10.3.7.1 XML Details**

2141 The following XML snippet depicts the sequence number as required in the transition mapping
 2142 message.

```

2143       <componentOf1>
2144        <sequenceNumber value="1"/>
2145        <submission>
2146        ...
2147        [Additional information appears for the submission element. Specific contents are defined in
2148        Regional/Module 1 Implementation Guide]
2149        ...
2150        <componentOf>
2151        ...
2152        [Additional information appears for the application element. Specific contents are defined in
2153        Section 8.2.10 and Regional/Module 1 Implementation Guide]
2154        ...
2155        </componentOf>
2156        </submission>
2157        </componentOf1>
  
```

2158 **10.3.7.2 XML Elements**

2159 The following table provides a complete set of XML elements and attributes required for the
 2160 *componentOf.sequenceNumber* element, and any special instructions.



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

2161

2162 **10.3.7.2.1 sequenceNumber**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>sequenceNumber</i>		[1..1]		This is the container element for the sequence number and its value.
	<i>value</i>	[1..1]	Numeric <i>e.g., 1, 2, 3.</i>	The <i>value</i> attribute of the <i>sequenceNumber</i> element provides a whole number to be used to order Submission Unit's within a Submission element.
<i>Conformance</i>	<i>sequenceNumber@value</i> attribute is required.			
<i>Business Rules</i>	The <i>sequenceNumber</i> is a positive integer. The values should begin with "1" and increment by whole numbers. The value should not be greater than "999999".			

2163 **10.3.8 Submission**

2164 The Submission element is described in Regional/Module 1 Implementation Guides, however for the
2165 purposes of the Current View Transition message the ICH Controlled Vocabulary should be used.

2166 **10.3.9 Technical Contact**

2167 A Transition Mapping submission file should include a technical contact party for the purposes of
2168 troubleshooting any issues with the forward compatibility file. The following information should be
2169 sent for each technical contact.

2170 **10.3.9.1 XML Details**

2171 The following tables provide a complete set of XML elements and attributes required for the
2172 *contactParty* element, and any special instructions.

2173 **10.3.9.2 XML Elements**

2174

2175 **10.3.9.2.1** *callBackContact.contactParty.id*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>id</i>		[1..1]		This is a container element that organizes the contact party's identifier.
	<i>root</i>	[1..1]	Valid UUID	This attribute is for a global unique identifier.
<i>Business Rules</i>	Contact Party identifier is required if the element is provided.			

2176 **10.3.9.2.2** *callBackContact.contactParty.code*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is a container element that organizes the coded value for the Contact Party
	<i>code</i>	[1..1]	Alpha Numeric	The code is a unique value that indicates the type of Contact Party based on Regional controlled vocabulary
	<i>codeSystem</i>	[1..1]	Valid OID	The codeSystem is a unique identifier that indicates the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
<i>Business Rules</i>	If a contact party is provided, a code value should be provided – e.g., for the technical contact.			

2177

2178 **10.3.9.2.3** *callBackContact.contactParty.statusCode*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is a container element that organizes the status code value for the Contact Party
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., active</i>	The code is a unique value that indicates the status of the Contact Party, and is based on HL7 controlled vocabulary.
<i>Business Rules</i>		Contact Party code is required if the element is provided.		

2179 **10.3.9.2.4** *callBackContact.contactParty.contactPerson.name*

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>item.part</i>		[1..1]		This is a container element that organizes the value of applicant's address.
	<i>value</i>	[1..1]	String <i>e.g., Jane</i>	This attribute is for the value of the name part of the Contact Party.
	<i>type</i>	[1..1]	Alpha <i>e.g., GIV</i> * note this is a controlled list from HL7 and included in the schema	This attribute is for the type of the name part – <i>e.g., family name or given name.</i>
<i>Business Rules</i>		Each part of a person's name will have its own <i>item</i> element.		

2180 **10.3.9.2.5** *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 <i>Examples</i>	Description <i>Instructions</i>
<i>item</i>		[1..1]		This is a container element that organizes the Contact Party’s contact information (e.g., telephone and email)
	<i>value</i>	[1..1]	String <i>e.g.,</i> tel:+1(111)999-9999	This attribute is for the value of the Contact Party’s contact information (e.g., telephone and email)
<i>Business Rules</i>	<p>The phone number value should follow the following format:</p> <ul style="list-style-type: none"> • 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”. <ul style="list-style-type: none"> ○ 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”. <ul style="list-style-type: none"> ○ For example “tel:+011(123)1234567890” or if no phone city, tel:+011()1234567890 <p>The email value should follow the following format:</p> <ul style="list-style-type: none"> • <i>value</i> should be formatted as: “mailto:johndoe@acme.com” 			

2181 **10.3.10 XML Sample: Technical Contact**

2182 The following XML snippet shows only the technical contact for the transition mapping message.
2183 Refer to Regional/Module 1 Implementation Guides for additional information on contacts for a
2184 regulatory activity.

```

2185 <callBackContact>
2186   <contactParty>
2187     <id root="20b45e49-a226-4bd4-a716-bb54eba3b0ec"/>
2188     <code code="ich technical" codeSystem="2.16.840.1.113883.3.989.2.2.4.1"/>
2189     <statusCode code="active"/>
2190     <contactPerson>
2191       <name>
2192         <part type="GIV" value="Joe"/>
2193         <part type="FAM" value="Smith"/>

```

```

2194         </name>
2195         <telecom xsi:type="BAG_TEL">
2196             <item value="tel:+1(111)999-9999"/>
2197             <item value="mailto:johndoe@acme.com"/>
2198         </telecom>
2199         <asAgent>
2200             <representedOrganization>
2201                 <name>
2202                     <part value="Acme Pharmaceuticals, Inc."/>
2203                 </name>
2204             </representedOrganization>
2205         </asAgent>
2206     </contactPerson>
2207 </contactParty>
2208 </callbackContact>

```

2209 10.3.11 Application

2210 The Application element is critical in defining which application will is relevant to the transition
 2211 mapping message. All validation rules will be completed based on the information provided for this
 2212 element.

2213 10.3.11.1 XML details

2214 The following is an example of the XML for the application information. The application enters as a
 2215 **componentOf** element between *submission* and *application*.

2216 ...[This XML section will repeat for each **application** element. A **submission** element is a **componentOf** an
 2217 **application** element]

```

2218 ...
2219 <componentOf>
2220     <application>
2221         <id>
2222             <item root="f23c558f-cd58-41bc-bf6f-c6d230d3d665" extension="987654"/>
2223         ...
2224         <!--Additional item elements can be added here-->
2225         ...
2226     </id>
2227     <code code="C72899" codeSystem="2.16.840.1.113883.3.26.1.1"/>

```

2228 ...
 2229 [Additional information may appear after the addition of the **application.code**, for
 2230 example any of the following elements related to **application** – **component**,
 2231 **referencedBy**, **informationRecipient**, **reference**, **subject**, or **holder**]

```

2232     ...
2233 </application>
2234 </componentOf>

```

2235



See [XML Color Legend](#) for color usage

2236 **10.3.11.2 XML Elements**

2237 The following tables provide a complete set of XML elements and attributes required for the
 2238 **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.

2239 **10.3.11.2.1 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..*]		This is the container element of the following attributes by which it uniquely identifies the application, because an application can be given multiple identifiers across territories, one id.item element should be used for each unique application identifier.
	root	[1..1]	Valid UUID	The root attribute of the id element provides a global unique identifier.
	extension	[0..1]	Alpha Numeric <i>e.g., 123456 (U.S. NDA value)</i>	The extension attribute of the id element provides a location to specify a region-specific application tracking number.
Conformance	The id.item@root attribute is required for the application element.			
Business Rules	Refer to Regional/Module 1 Implementation Guides.			

2240

2241 **10.3.11.2.2 application.code**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
<i>code</i>		[1..1]		This is the container element that organizes the coded value for the application.
	<i>code</i>	[1..1]	Alpha Numeric <i>Terminology is specified by the appropriate Regional/ Module 1 Implementation Guide.</i>	The <i>code</i> attribute is a unique value that indicates the type of content in the application based on regional controlled vocabulary (e.g., NDA, MAA, Art-8-3, Art-10-1, etc.).
	<i>codeSystem</i>	[1..1]	Valid OID	The <i>codeSystem</i> attribute is a unique identifier that indicates the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
<i>Conformance</i>	There must be one and only one <i>code@code</i> attribute specified for an application.			
<i>Business Rules</i>	The code value must match the value for the existing application.			

2242 **10.3.12 Document**

2243 The *document* element is the link to v3.2.2 leaf elements – this is critical to enabling document reuse
 2244 in v4.0 messages. The current v3.2.2 implementation may include the same file referenced in
 2245 multiple leafs within or across applications. The applicant should decide how to deal with the
 2246 definition of a document object – specifically the document identifier. For optimal document reuse –
 2247 a file would have one and only one document identifier. If this is not executed – the applicant will
 2248 need to manage the submission contents and determine which document to reuse in the future. Once
 2249 a document identifier is established – the version 4.0 document identifier may also be referenced
 2250 multiple times in the application transition message or future application transition mapping
 2251 messages.

2252 **10.3.12.1 XML Elements**

2253 The following tables provide a complete set of XML elements and attributes required for the
 2254 *document* element, and any special instructions.



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

2255 **10.3.12.1.1 document.id**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>id</i>		[1..1]		This is the container element for the document identifier.
	<i>root</i>	[1..1]	Valid UUID	This <i>root</i> attribute of the <i>id</i> element is a global unique identifier of the <i>document</i> .
<i>Conformance</i>	The <i>root</i> is a required attribute.			
<i>Business Rules</i>	The <i>id@root</i> should be unique for every <i>document</i> element, i.e., there should not be two documents submitted with the same <i>id@root</i> value.			

2256 **10.3.12.1.2 document.text**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>text</i>		[0..1]		This is the container element that provides additional information about the document.
<i>text.reference</i>		[0..1]		This is the container element within the <i>text</i> element for a document.
	<i>value</i>	[1..1]	Alpha Numeric <i>Leaf Reference based on URI algorithm</i>	This is the <i>value</i> attribute of the <i>text</i> element that provides the location of the document with the relative path and filename of the document.
<i>Conformance</i>	Documents require the following elements/attributes: <ul style="list-style-type: none"> • The <i>text</i> element <ul style="list-style-type: none"> ○ The <i>reference@value</i> attribute 			
<i>Business Rules</i>	The <i>text</i> element should be used to send the leaf reference with the designated URI algorithm -- SequenceNumber.xmltype.leafId (e.g., 0032.ich#NLAS57D17EB601C9EDCA)			

2257 **10.3.13 XML SAMPLE: Transition mapping of Document elements**

2258 The following is an example of the XML for the Document element for the transition mapping
 2259 message.

2260 **Document Element**

```

2261 <component>
2262 <document>
2263 <id root="fe5fcddd-397b-4042-8fc8-c6163e76bab2"/>
2264 <text>
2265 <reference value="0032.ich#NLAS57D17EB601C9EDCA"/>
2266 </text>
2267 </document>
2268 </component>
2269
  
```

2270 **10.3.13.1 Keyword Definition**

2271 Only the existing 3.2.2 keywords defined by the user, i.e., *keywordDefinition* should be provided in
 2272 the transition mapping message for the existing leaf elements in the v3.2.2. Additional keyword
 2273 definitions will be addressed by Regional/Module 1 Implementation Guides if they are submitted and
 2274 not used as keywords.

2275 **10.3.13.2 XML Elements**

2276 The following tables provide a complete set of XML elements and attributes required for the
 2277 *keywordDefinition* 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.

2278 Each *keywordDefinition* should be sent in its own *keywordDefinition* element. Although the schema
 2279 allows multiple values for each *keywordDefinition*, the eCTD v4.0 only allows one item per
 2280 *keywordDefinition* element.

2281 **10.3.13.2.1 keywordDefinition.code**

Element	Attribute	Cardinality	Value(s) Allowed Examples	Description Instructions
<i>code</i>		[1..1]		This is the container element that identifies the type of keyword definition.
	<i>code</i>	[1..1]	Alpha Numeric <i>e.g., “ich- manufacturer ”</i>	This is the <i>code</i> attribute for the coded value of the type of keyword definition.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
	codeSystem	[1..1]	Valid OID	This is the codeSystem OID that is a unique identifier for the controlled vocabulary system. <i>This should be the OID registered for the code system.</i>
Conformance	The code and codeSystem are required attributes.			
Business Rules	The code must be from a valid ICH Keyword code type.			

2282 **10.3.13.2.2 keywordDefinition.statusCode**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
statusCode		[1..1]		This is the container element that identifies the status of the keywordDefinition .
	Code	[1..1]	Alpha <i>e.g., active</i>	This is the code value for the status.
Conformance	The statusCode is required.			
Business Rules	The code attribute should always have a value of “active”.			

2283 **10.3.13.2.3 keywordDefinition.value**

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
value		[1..1]		This is the container element for the keyword defined for the keyword code provided for keywordDefinition .
value.item		[1..1]		This is the container element to specify an individual keyword identifier.

Element	Attribute	Cardinality	Value(s) Allowed <i>Examples</i>	Description <i>Instructions</i>
	Code	[1..1]	Alpha Numeric Sender specified value <i>e.g., MANU001</i>	This is the code attribute for the keyword being defined.
	codeSystem	[1..1]	Valid OID	This is the codeSystem OID that is a unique identifier for the controlled vocabulary system.
value.item.displayName		[1..1]		This is the container element to specify the displayName , which is the value of the keywordDefinition code.
	value	[1..1]	Alpha Numeric <i>Sender specified value e.g., “Big Manufacturer”</i>	The displayName attribute of the value element of the keyword being defined.
Conformance	The keywordDefinition.value is a required element. The value.item@code , value.item@codeSystem and value.item.displayName@value are required attributes.			
Business Rules	Each keywordDefinition can only contain one sender-specified keyword. Each value.item@code and value.item.displayName@value combination must match an existing v3.2.2 attribute type and value.			

2284 **10.3.14 XML SAMPLE: Transition mapping of Keyword Definitions**

2285 The following XML sample shows one **keywordDefinition** of type, product name.

```

2286
2287     <referencedBy>
2288         <keywordDefinition>
2289             <code code="ich keyword type 4"
2290                 codeSystem="2.16.840.1.113883.3.989.2.2.4.1.2"/>
2291             <statusCode code="active"/>

```

```
2292         <value>
2293             <item code="PRD-001" codeSystem="CompanyOID-ProductKeyword">
2294                 <displayName value="Product A"/>
2295             </item>
2296         </value>
2297     </keywordDefinition>
2298 </referencedBy>
```

2300 Note: that one item value per keyword definition is required; the schema allows for multiple.
2301



See [XML Color Legend](#) for color usage.

2302

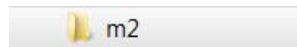
2303 **11. APPENDIX 1: SAMPLE FILES AND FOLDERS FOR MODULES 2-5**

2304 With increased document reuse in eCTD v4.0, the folder structure will no longer serve as a reliable
2305 mechanism to navigate through the submission content. The folder structure for Modules 2-5 is
2306 presented below. Additional folders should only be included for technical reasons (e.g., providing
2307 files with the same name) and should only be placed at the lowest level of the folder structure as
2308 specified in each of the subsections below.

2309 **11.1 Module 2 Summaries**

2310 The files in this module should be provided as PDF text with the exception of a few embedded
2311 images, when needed. The name of the folder for module 2 should be m2. No additional folders are
2312 necessary in this module. The m2 folder structure is depicted in Figure 4: Module 2 Folder Structure
2313 as a single folder.

2314 **Figure 4: Module 2 Folder Structure**



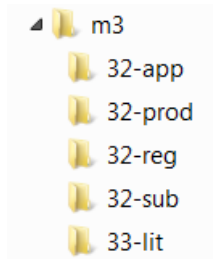
2315
2316

2317 **11.2 Module 3 Quality**

2318 The name of the folder for module 3 should be m3. The folders in module 3 should be named as
2319 follows but can be further reduced or omitted to minimize path length issues. Additional folders
2320 should only be provided to organize files with the same name.

2321 The m3 folder structure is depicted in Figure 5: Module 3 Folder Structure.

2322 **Figure 5: Module 3 Folder Structure**



2323

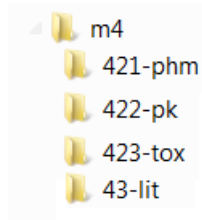
Section in CTD	Description	Folder Name
3.2.A	Appendices	<i>32-app</i>
3.2.P	Drug Product (name, dosage form)	<i>32-prod</i>
3.2.R	Regional Information	<i>32-reg</i>
3.2.S	Drug Substance	<i>32-sub</i>
3.3	Literature References	<i>33-lit</i>

2324

2325 **11.3 Module 4 Nonclinical Study Reports**

2326 The name of the folder for module 4 should be m4. The folders in module 4 should be named as
2327 follows but can be further reduced or omitted to minimize path length issues. The m4 folder structure
2328 is depicted in Figure 6: Module 4 Folder Structure.

2329 **Figure 6: Module 4 Folder Structure**



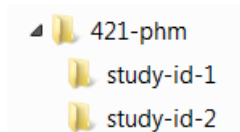
2330

Section in CTD	Description	Folder Name
4.2.1	Pharmacology	<i>421-phm</i>
4.2.2	Pharmacokinetics	<i>422-pk</i>
4.2.3	Toxicology	<i>423-tox</i>
4.3	Literature References	<i>43-lit</i>

2331

2332 Additional folders may be added to organize study files, which may be required to allow multiple
2333 files with the same name. The folders should be named with the study identifier number (e.g., study-
2334 id-1) as depicted in Figure 7: Example of Study folders. Refer to Regional/Module 1 Implementation
2335 Guides for rules additional folders in this module.

2336 **Figure 7: Example of Study folders**



2337

2338 **11.4 Module 5 Clinical Study Reports**

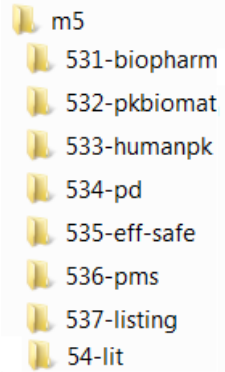
2339 The name of the folder for module 5 should be m5. The folders in module 5 should be named as
2340 follows but can be further reduced or omitted to minimize path length issues.

- 2341 • The CTD organization provides locations for case report forms and individual patient data
2342 listings in Module 5.3.7. See Regional/Module 1 Implementation Guides for additional
2343 guidance for case report forms, data sets and individual patient data listings
- 2344 • In the eCTD v4.0, files for publications and literature references should be located in the
2345 folder for Module 5.4.

2346 The m5 folder structure is depicted in Figure 8: Module 5 Folder Structure

2347

Figure 8: Module 5 Folder Structure



2348

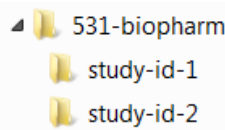
Section in CTD	Description	Folder Name
5.3.1	Reports of Biopharmaceutic Studies	<i>531-biopharm</i>
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	<i>532-pkbiomat</i>
5.3.3	Reports of Human Pharmacokinetic (PK) Studies	<i>533-humanpk</i>
5.3.4	Reports of Human Pharmacodynamic (PD) Studies	<i>534-pd</i>
5.3.5	Reports of Efficacy and Safety Studies	<i>535-eff-safe</i>
5.3.6	Reports of Postmarketing Experience	<i>536-pms</i>
5.3.7	Case Report Forms and Individual Patient Listings	<i>537-listing</i>
5.4	Literature References	<i>54-lit</i>

2349

2350 Additional folders may be added to organize study files, which may be required to allow multiple
 2351 files with the same name. The folders should be named with the study identifier number (e.g., study-
 2352 id-1) as depicted in Figure 9: Example of Study Folders. Refer to Regional/Module 1 Implementation
 2353 Guides for rules additional folders in this module.

2354

Figure 9: Example of Study Folders



2355

2356 **12. APPENDIX 2: VALIDATION OF THE eCTD v4.0 MESSAGE**

2357 The validation of the eCTD v4.0 message will not only include the general schema validation,
 2358 against the ICH eCTD v4.0 Schema, but also additional business rules that are documented in this
 2359 Implementation Guide and the Regional/Module 1 Implementation Guide.

2360 For specific conformance and business rules for the eCTD v4.0 message, refer to each element
 2361 specification in Section 8.2.

- 2362 • Conformance – these statements should be enforced by the schema, e.g., cardinality, but in
 2363 some cases the cardinalities have conditions and in certain situations, the element or
 2364 attribute are required. Those items will be specified in each of the Required XML Element
 2365 tables.
- 2366 • Business Rules – these are additional rules that are not enforced by the schema, but based
 2367 on consensus within ICH, these rules have been set for the eCTD v4.0 message. These
 2368 business rules will invoke additional requirements for regulatory authorities and regulated
 2369 industry.

2370 The remaining validation rules are found in this section of the document, both in summary and
 2371 detailed versions.

2372 **12.1 Summary of Validation Rules**

2373 The following section outlines the validation rules by type or element. Additional details are in
 2374 the subsections below.

Category	Type/Element	Validation Criteria
Message Validation	Schema	Message must be Well Formed XML based on XML 1.0.
		Message must be valid against the ICH specified version of the RPS schema
	Submission Unit	Submission Unit identifier is required (1..1)
		Submission Unit id root must be a unique identifier
		Only one Submission Unit element can exist for a message.
		Submission Unit code value is required (1..1)
		Submission Unit must have a valid code value
		Submission Unit Code System value is required (1..1)
		Submission Unit code must have a valid OID for the Code System value
	The Submission Unit status code requires the code attribute “active”	
	Sequence Number	Sequence Number is required (1..1)
		Sequence Number must be a whole number
		Sequence Number for initial submission unit starts with 1
		Sequence Number is unique in the application for the applicant
		The Sequence Number must have one and only one value for the Submission element
	Priority	CoU Priority Number is required

Category	Type/Element	Validation Criteria
	<u>Number (CoU)</u>	CoU Priority Number must be a non-negative real number
		CoU Priority Number shall have one and only one value
	<u>Context of Use</u>	CoU identifier is required
		CoU id root must be a unique identifier
		CoU status code element is required
		CoU status code value can only be “active” or “suspended”
	<u>Related Context of Use</u>	RelatedCoU identifier is required when RelatedCoU is provided
	<u>Document Reference</u>	DocumentReference identifier is required for all active CoU elements
		DocumentReference element not allowed for suspended CoU elements
	<u>Keyword</u>	Keyword code is required for each keyword element on a CoU
		Keyword code system is required for each keyword element
		Keyword code system must be a valid OID
		Keyword code system must have a valid value
	<u>Submission</u>	Submission identifier is required (1..1)
		Submission code is required (1..1)
		Submission code must have a valid value for the region
		Submission code system is required (1..1)
		Submission code system must have a valid regional code system OID
	<u>Application</u>	Application identifier is required (1..1)
		Application code is required
		Application code must have a valid value
		Application code system is required
		Application code system is a valid OID
	<u>Document</u>	Document identifier is required (1..1)
		Document id root must be a unique identifier
		Document identifier must have a valid value
		Document identifier is unique (i.e., it is not a duplicate identifier and not an update to a document title)
		Document title is required
		Document text element requires a checksum value unless a document title update is submitted (i.e., this is the only scenario making this element optional)
		Document text element requires a valid checksum value unless a document title update is submitted (i.e., this is the only scenario making this element optional)
		Document path is required unless the document title update is submitted (i.e., this is the only scenario making this element optional)

Category	Type/Element	Validation Criteria
		Document path does not exist unless the document title update is submitted (i.e., this is the only scenario making this element optional)
	<u>Keyword Definition</u>	Keyword definition code is required (1..1)
		Keyword definition code must have a valid value
		Keyword definition value code is required (1..1)
		Keyword definition value code must have a valid value
		Keyword definition value is required (1..1)
		Keyword definition value has one and only one value.item element
		Keyword definition display name value is required
Submission Package	<u>Submission Package</u>	Submission File Name
		Submission File quantity
		Submission File location
		File name format
		Document checksum is validated against the document's calculated checksum
		File name length
		Folder name length
		Folder path length

2375
2376
2377
2378

12.1.1 Message Validation Rules

These are validation criteria that can either be passed or failed. eCTDs that fail to meet one or more of these criteria will be returned to the applicant for correction and resubmission as the same sequence number.

No Unique ID	Category	Validation Criteria	Issue Description	Corrective Action
Schema				
eCTD 4-001	Schema	Message must be Well Formed XML based on XML 1.0.	The XML is not well-formed according to the version of the XML standard.	The XML must be corrected to become well-formed.
eCTD 4-002	Schema	Message must be valid against the ICH specified version of the RPS schema	The message is not valid against the current ICH specified version of the RPS schema	The XML should be corrected to meet all of the schema validations.
Submission Unit				
eCTD 4-003	Schema	Submission Unit identifier is required (1..1)	<i>SubmissionUnit.id@root</i> is not provided	The submission unit needs to be resubmitted with a value for <i>id@root</i> for the submission unit.
eCTD 4-004	Business Rule	Submission Unit id root must be a unique identifier	<i>SubmissionUnit.id@root</i> is not unique	The submission unit needs to be resubmitted with the unique identifier for the submission unit element.
eCTD 4-005	Business Rule	Only one Submission Unit element can exist for a message.	The message has more than one submission unit in a message payload	The submission unit needs to be resubmitted with only one submission unit included.
eCTD 4-006	Schema	Submission Unit code value is required (1..1)	The <i>SubmissionUnit.code@code</i> value is not provided	The submission unit needs to be resubmitted with a code value.
eCTD 4-007	Business Rule	Submission Unit must have a valid code value	The <i>SubmissionUnit.code@code</i> is not a valid value (for the region)	The submission unit needs to be resubmitted with a valid code value.
eCTD 4-008	Business Rule	Submission Unit Code System value is required (1..1)	The <i>submissionUnit.code@codeSystem</i> is not provided	The submission unit needs to be resubmitted with a valid code value.

No	Category	Validation Criteria	Issue Description	Corrective Action
eCTD 4-009	Schema	Submission Unit code must have a valid OID for the Code System value	The <i>submissionUnit.code@codeSystem</i> is not a valid registered or known OID	The submission unit needs to be resubmitted with a valid code system OID.
eCTD 4-010	Business Rule	The Submission Unit status code requires the code attribute “active”	The submission unit does not have a status code value of active	The submission unit needs to be resubmitted with an active status code.
Sequence Number				
eCTD 4-011	Business Rule	Sequence Number is required (1..1)	The sequence number value is not provided	The submission unit may need to be resubmitted with a sequence number.
eCTD 4-012	Business Rules	Sequence Number must be a whole number	The sequence number value is not a whole number	The submission unit may need to be resubmitted with a correctly formatted sequence number
eCTD 4-013	Business Rule	Sequence Number for initial submission unit starts with 1	The sequence number for the initial submission unit in an application does not start with 1.	The submission unit needs to be resubmitted with the sequence number starting with 1.
eCTD 4-014	Business Rule	Sequence Number is unique in the application for the applicant	The sequence number is not unique in a submission/application	The submission unit needs to be resubmitted to make the sequence number unique for the application.
eCTD 4-015	Business Rule	The Sequence Number must have one and only one value for the Submission element	The Sequence Number does not have one and only one value for each Submission in the submission unit.	The submission unit needs to be resubmitted providing a value. The submission unit needs to be resubmitted to be different than the values that exist for the submission/ application.
Priority Number				
eCTD 4-016	Schema	CoU Priority Number is required	The priority number value is not provided.	The submission unit would need to be resubmitted providing priority numbers.

No Unique ID	Category	Validation Criteria	Issue Description	Corrective Action
eCTD 4-017	Business Rules	CoU Priority Number must be a non-negative real number	The priority number value is not a non-negative real number	The submission unit would need to be resubmitted with non-negative real numbers for the priority number value.
eCTD 4-018	Schema	CoU Priority Number shall have one and only one value	There is more than one CoU priority number provided for each CoU	The submission unit would need to be resubmitted providing priority numbers.
Context of Use				
eCTD 4-018	Schema	CoU identifier is required	The <i>ContextOfUse.id@root</i> is not provided	The submission unit needs to be resubmitted providing a CoU identifier.
eCTD 4-019	Schema	CoU id root must be a unique identifier	The <i>ContextOfUse.id@root</i> value is not unique	The submission unit needs to be resubmitted with a unique CoU identifier.
eCTD 4-020	Schema	CoU status code element is required	The CoU statusCode element is not provided.	The submission unit needs to be resubmitted with a status code for each CoU.
eCTD 4-021	Schema	CoU status code value can only be “active” or “suspended”	The <i>CoUstatusCode@code</i> value is not “active” or “suspended”.	The submission unit needs to be resubmitted with a valid status code for the CoU.
Related Context of Use				
eCTD 4-022	Schema	RelatedCoU identifier is required when RelatedCoU is provided	<i>RelatedCoU.id@root</i> attribute is not provided.	The submission unit needs to be resubmitted providing a relatedCoU identifier.
Document Reference				
eCTD 4-023	Business Rule	DocumentReference identifier is required for all active CoU elements	<i>DocumentReference.id@root</i> attribute is not provided when the Context of Use is active	The submission unit needs to be resubmitted with a Document Reference identifier when the CoU is active.

No	Category	Validation Criteria	Issue Description	Corrective Action
eCTD 4-024	Schema	DocumentReference element not allowed for suspended CoU elements	Document Reference element is provided when the Context of Use is suspended	The submission unit needs to be resubmitted without a Document Reference when the CoU is suspended.
Keyword				
eCTD 4-025	Schema	Keyword code is required for each keyword element on a CoU	<i>Keyword.code@code</i> attribute is not provided.	The submission unit needs to be resubmitted providing a Keyword code for each CoU.
eCTD 4-026	Schema	Keyword code system is required for each keyword element	The <i>Keyword.code@codeSystem</i> is not provided.	The submission unit needs to be resubmitted providing a Keyword code system for each Keyword code.
eCTD 4-027	Schema	Keyword code system must be a valid OID	<i>Keyword.code@codeSystem</i> is not a valid registered or known OID	The submission unit needs to be resubmitted with a valid keyword code system.
eCTD 4-028	Business Rule	Keyword code system must have a valid value	The keyword code is not part of the external controlled vocabulary or defined in the application's keyword definitions	The submission unit needs to be resubmitted with a valid code system for the keyword code.
Submission				
eCTD 4-029	SchemaRules	Submission identifier is required (1..1)	Submission <i>id@root</i> is not provided.	The submission unit needs to be resubmitted with a submission identifier.
eCTD 4-030	SchemaRules	Submission code is required (1..1)	<i>Submission.code@code</i> attribute is not provided	The submission unit needs to be resubmitted providing a Submission code.
eCTD 4-031	Business rules	Submission code must have a valid value for the region	<i>Submission.code@code</i> is not a valid value.	The submission unit needs to be resubmitted with valid Submission code.

No	Category	Validation Criteria	Issue Description	Corrective Action
Unique ID				
eCTD 4-032	Schema	Submission code system is required (1..1)	<i>Submission.code@code System is</i> not provided	The submission unit needs to be resubmitted providing a Submission code system.
eCTD 4-033	Business rules	Submission code system must have a valid regional code system OID	<i>Submission.code@code System</i> is not a valid, registered or known OID	The submission unit needs to be resubmitted with a valid Submission code system.
Application				
eCTD 4-034	Schema	Application identifier is required (1..1)	<i>Application.id.item@root</i> is not provided.	The submission unit needs to be resubmitted with an application identifier.
eCTD 4-035	Schema	Application code is required	<i>Application.code@code</i> attribute is not provided.	The submission unit needs to be resubmitted providing an Application code.
eCTD 4-036	Business Rule	Application code must have a valid value	<i>Application.code@code</i> is not a valid value.	The submission unit needs to be resubmitted with a valid Application code value.
eCTD 4-037	Schema	Application code system is required	<i>Application.code@code System</i> is not provided.	The submission unit needs to be resubmitted providing an Application code system.
eCTD 4-038	Business Rule	Application code system is a valid OID	<i>Application.code@code System</i> is not a valid OID. If the OID does not link to a valid code system and value, the information may not be interpretable.	The submission unit needs to be resubmitted with a valid Application code system.
Document				
eCTD 4-039	Schema	Document identifier is required (1..1)	Document <i>id@root</i> is not provided	The submission unit needs to be resubmitted providing the Document identifier.

No	Category	Validation Criteria	Issue Description	Corrective Action
eCTD 4-040	Business Rules	Document identifier must have a valid value	The document identifier is not a valid value.	The submission unit needs to be resubmitted with a corrected valid document identifier.
eCTD 4-062	Business Rules	Document id root must be a unique identifier	The <i>Document.id@root</i> value is not unique	The submission unit needs to be resubmitted with a unique Document identifier.
eCTD 4-041	Business Rules	Document identifier is unique (i.e., it is not a duplicate identifier)	The document identifier is not unique.	The submission unit needs to be resubmitted with a correction to the unique identifier.
eCTD 4-042	Business Rules	Document title is required	Document <i>document.title@value</i> does not have a value or does not exist.	The submission unit needs to be resubmitted with a corrected document title value for all documents
eCTD 4-043	Business Rules	Document text element requires a checksum value	The <i>document.text.integrity Check</i> value is not provided for the document element	The submission unit needs to be resubmitted with a checksum value for all documents
eCTD 4-044	Business Rules	Document text element requires a valid checksum value	The document <i>document.text.integrity Check</i> value is not a valid checksum	The submission unit needs to be resubmitted with a valid checksum value for all documents
eCTD 4-045	Schema	Document path is required	The <i>document.text.reference @value</i> is not provided	The submission unit needs to be resubmitted with a document path for all documents
eCTD 4-046	Business Rule	Document path does not exist	The document path provided in the eCTD XML does not physically exist	The submission unit needs to be resubmitted with a correct document path.
Keyword Definition				
eCTD 4-047	Business Rule	Keyword definition code is required (1..1)	The <i>keywordDefinition.code @code</i> is not provided	The submission unit needs to be resubmitted with a keyword definition code

No	Category	Validation Criteria	Issue Description	Corrective Action
Unique ID				
eCTD 4-048	Business Rule	Keyword definition code must have a valid value	The <i>keywordDefinition.code@code</i> is not a valid value	The submission unit needs to be resubmitted with a valid keyword definition code
eCTD 4-049	Business Rule	Keyword definition value code is required (1..1)	The <i>keywordDefinition.value.item@code</i> is not provided	The submission unit needs to be resubmitted with a keyword definition value code
eCTD 4-050	Business Rule	Keyword definition value code must have a valid value	The <i>keywordDefinition.value.item@code</i> is not a valid value	The submission unit needs to be resubmitted with a valid keyword definition value code
eCTD 4-051	Business Rule	Keyword definition value is required (1..1)	The <i>KeywordDefinition.value</i> element is not provided	The submission unit needs to be resubmitted with a valid keyword definition value
eCTD 4-052	Business Rule	Keyword definition value has one and only one value.item element	More than one <i>KeywordDefinition.value.item</i> element is provided	The submission unit needs to be resubmitted with a one <i>value.item</i> element per keyword definition value
eCTD 4-053	Business Rule	Keyword definition display name value is required	The <i>KeywordDefinition.value.item.displayName@value</i> is not provided.	The submission unit needs to be resubmitted providing a <i>keywordDefinition.value.item.displayName@value</i>

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12.1.2 Submission Package Validation Rules

No	Category	Validation Criteria	Issue Description	Corrective Action
Unique ID				
eCTD 4-054	Business Rule	Submission File Name	The submission file name is not submissionunit.xml	The filename should be corrected to the specified naming convention required for eCTD v4.x.
eCTD 4-055	Business Rule	Submission File quantity	There is more than one submissionunit.xml file included in the submission package.	The submission unit needs to be resubmitted with just one submissionunit.xml file.

No Unique ID	Category	Validation Criteria	Issue Description	Corrective Action
eCTD 4-056	Business Rule	Submission File location	The submissionunit.xml file is not placed at the correct location in the folder structure to be detected by receiving systems	The submission unit needs to be resubmitted with the submissionunit.xml placed in the top-level of the directory of the submission contents package.
eCTD 4-057	Business Rule	File name format	The file does not follow the naming convention instructions – i.e., lower case is not used	The submission unit needs to be resubmitted with the correct file naming convention for all documents.
eCTD 4-058	Business Rule	Document checksum is validated against the document's calculated checksum	The Document checksum(s) of eCTD XML (see validation rules for message – specifically the text element) is not the same as checksum of the file in the folder	The submission unit needs to be resubmitted with the correct checksum for the submitted document.
eCTD 4-059	Business Rule	File name length	The file name length exceeds the allowable number of characters. Note: 64 characters allowed	The submission unit needs to be resubmitted with file names that meet the 64 character limit.
eCTD 4-060	Business Rule	Folder name length	The folder name length exceeds the allowable number of characters. Note: 64 characters allowed	The submission unit needs to be resubmitted with folder names that meet the 64 characters allowed.
eCTD 4-061	Business Rule	Folder path length	The folder path length exceeds the allowable number of characters. Note: 180 characters allowed	The submission unit needs to be resubmitted with the folder path within the 180 characters allowed.

2380 **13. APPENDIX 3 SAMPLE ECTD MESSAGES**

2381 Refer to Regional/Module 1 Implementation Guides for complete eCTD sample messages.

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