

Electronic Common Technical Document (eCTD) v4.0 EU Module 1 Implementation Guide

**DRAFT for Updates 2024**

Version 1.1

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**DOCUMENT CHANGE HISTORY**

|  |  |  |
| --- | --- | --- |
| **Version** | **Date** | **Comments** |
| 0.1 | 6th Jan 2012 | First draft based on ICH eCTD IG v3.1 deleting all M2 to 5 specifics and adding all EU Module 1 details, e.g. controlled vocabularies and content from the current EU Module 1 specification as far as possible, except  updating all XML snippets and XML elements tables. |
| 0.2 | 16th Jan 2012 | Update based on ICH eCTD IG v4.0 |
| 0.3 | 15th Feb 2012 | Update based on ICH eCTD IG v5.0, correction of CV on EU Application Type, EU Contact Party, EU Regulatory Status, deletion of non EU specific  information on life cycle management |
| 0.4 | 22nd Feb 2012 | Deleting all doubled XML tables but referencing to  ICH eCTD IG. Note: XML tables are frequently copied and not yet checked for consistency. |
| 0.5 | 1st Mar 2012 | Update covering M8 TC 29 Feb 2012, comments from  Andreas Franken |
| 0.6 | 2nd March 2012 | Replace of most of the XML snippets by the following note:  *Note: Examples for XML snippets will be provided in one of the future versions* |
| 0.7 | 15th April 2012 | Incorporate comments from vendors and adjusting text according ICH eCTD IG v6.0. A number of XML  snippets have been added. Business scenarios in new section 9.2 |
| 0.8 | 30th April 2012 | Incorporate changes based on ICH eCTD IG v7.0, add more XML samples and outline missing business  scenarios, add new section on message created by regulators, re-numbering of sections as appropriate. |
| 0.81 | 18th May 2012 | Layout and editorial changes, deletion of duplications,  consistency improvement. |
| 0.82 | 10th June 2012 | Editorial changes, including confirmations after TIGes Meeting 25.05.2012, incorporate changes based on Draft ICH eCTD IG for Testing v 1.0, clarification on  sequence number use |
| 1.0 | 30th June 2012 | Release for public consultation and testing purpose |
| 1.01 | 15th Nov 2014 | Update after HL7 normative ballot and finalisation of  ICH Step 2 |
| 1.02 | 30th Dec 2014 | Accepting all changes so far for preparing the work within the eCTD v4.0 Maintenance Group. Including some changes following the review of the draft USFDA  regional IG, dated 16.12.2014 |
| 1.03 | 06th Jan 2015 | Revision of chapter 5, deletion of section 5.9 |
| 1.04 | 13th Jan 2015 | Group Review of Chapters 1 to 5, mostly editorial |

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| --- | --- | --- |
|  |  | changes. |
| 1.05 | 21st Jan 2015 | Consolidating comments and text improvements of  Chapters 1 to 3, change of Section 6.1 into a table |
| 1.06 | 27th Jan 2015 | Consolidating comments and improvements, additional comments by AJ, AD, LS, correction of XML location  stats |
| 1.07 | 23rd Feb 2015 | Completing the first folder naming conventions for grouping and worksharing. Source added of CTL EU Territorial Authority and CTL EU Procedural Authority Role. Review of XML snippets. Correction of XML details of the ***document*** element. Addition of sample of grouped variation. Constraining the validation criteria  to its minimum. |
| 1.08 | 9th March 2015 | Review of XML snippets |
| 2.0 | 10th Mar 2015 | Release for public consultation |
| 2.1 |  | Correction of typos, comments from ICH IG discussion |
| 2.2 | 19th May 2016 | Revision to adapt to ICH IG (final version as of  31 March 2016), including XML snippets |
| 2.3 | 28th July 2016 | Consolidation of comments |
| 2.4 | 23rd Aug 2016 | Addition of XML samples |
| 2.5 | 10th Nov 2016 | Accepting changes made by LS, additions regarding  root folder name, consolidating alongside with ICH IG v1.2 |
| 2.6 | 10th Mar 2017 | Consolidating entire document, including OIDs and UUIDs in accordance with already available information details, completing XML snippets (not yet reviewing the complex samples and separate the  annexes). Linguistic review. Updating links. Formating |
| 2.7 | 11th Apr 2017 | Restrict managing options for groupings and  worksharing to simple Submission Unit xml files. Review of XML snippets grammar. |
| 2.8 | 18th May 2017 | Corrections after eCTDv4.0 MG review |
| 2.9 | 19th Mar to 5th  September 2018 | Changes following public consultation, discussion with  ICH M8 and review by eCTD4.0 MG |
| 1.0 | 11th October 2018 | Final version for implementation and re-set of version numbering, assigning OID  2.16.840.1.113883.3.989.5.1.1.6.1.1 |
| 1.1 | 15th of March 2024 | **Comprehensive revision** |

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# NOTICE TO READER

Sections of this document referencing the Health Level Seven (HL7) Version 3Standard: Regulated Product Submission Release 2 Normative are used with the publisher’s permission. The HL7 Standard (Version 3) Regulatory Product Submission Release 2 Normative is copyrighted by Health Level Seven International ® ALL RIGHTS RESERVED

# INSTRUCTIONS TO READER

This is a technical document that provides instructions on how to implement the eCTD v4.0 specification for European purposes. The following content will be provided in a consistent manner within the document and/or the reader may be prompted by visual cues about the context or referenced information being presented in the document.

This document needs to be read in conjunction with the ICH Implementation Guide on electronic Common Technical Document Version 4.0.

For further instructions, please consult the ICH Implementation Guide on electronic Common Technical Document Version 4.0.

Please be aware, that all XML samples have been created manually and may not be entirely correct or can be used by any software without careful control. For the final version of the Implementation Guide, it is expected that all XML snippets can be built by software.

For the colour coding used in the XML snippets, please consult the ICH Implementation Guide.

***Note:*** *All UUIDs and OIDs used in the XML samples and snippets are only for illustrational purposes, to demonstrate how the respective XML section will look. They cannot be used for testing. They will be replaced by real values once these are available.*

***All OIDs are currently under review and they are subject to change. For this reason, they are marked with a different style in the document and they will be updated before publishing the final version of the EU Implementation Guide.***

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

Table : Legend of Symbols used in Document

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

# PURPOSE AND SCOPE

This document serves as the Implementation Guide (IG) and a technical specification for the regional EU Module 1 of the Electronic Common Technical Document (eCTD) v4.0 using the HL7 Version 3 Regulated Product Submission (RPS) Release 2 Normative for human medicinal products. Applicable information indicated in the ICH eCTD IG[[1]](#footnote-2)to be regionally available is incorporated as necessary to assist in the system development requirements for publishing or displaying eCTD v4.0 compliant messages for the recipients of the information.

The RPS standard defines the message for exchanging regulatory information electronically between Competent Authorities and the Pharmaceutical Industry as well as between Competent Authorities in general and needs to be detailed by implementation guides. This document only comprises the EU Module 1 part of the eCTD XML message including the Regional Administrative and EU-specific Product Information. The focus is to outline the essential components of the message which are required for EU Module 1 in addition to and/or differently from the common CTD Modules 2 – 5.

The content of eCTD v4.0 Modules 2 - 5, being shared across all regions represented in the International Council of Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), is not included in this IG, although some principles need to be repeated in the document to assure a better understanding. This document therefore should be read together with the ICH eCTD IG to prepare a valid eCTD Submission Unit in the EU.

In addition, relevant rules and examples are provided to enable transition from eCTD v3.2.2 to v4.0.

# MAJOR CHANGES AND ADVANTAGES OF ECTD V4.0

The Pharmaceutical Industry and Competent Authorities, which serve to regulate Industry, exchange information to address a variety of regulatory processes. The scope of the ICH activities covers the human pharmaceutical product marketing authorisation processes. The eCTD format is the mandatory electronic submission format that is accepted by the European Medicines Agency[[2]](#footnote-3) (hereafter referred to as EMA) and all National Competent Authorities (hereafter referred to as NCAs).

The use of an international information exchange standard is needed in the regulatory environment to ensure that mandates can be issued, and standardisation enabled for

increased consistency across the competent authorities with respect to the exchange of regulatory information.

As the eCTD is regarded as the principal electronic submission format in the EU, the goal of the upgrade to 4.0 is to significantly enhance the capability of eCTD to facilitate the processing and review of electronic regulatory submissions. Examples of enhancement features and the re-use of data are in the ‘context of use’ which will allow one piece of data to be used across many applications, avoiding the need for duplication of data elements.

The new version of the eCTD implementation based on the HL7 RPS Standard will offer:

* + Options to accommodate regulatory changes without delay and major technical changes as content related changes can be achieved by updates of controlled vocabularies or modification of keywords
  + Applicability of the same technology for all types of regulated products
  + Use of controlled vocabularies to a wide extent
  + Use of keywords for organising content
  + Improvement of life cycle operations by simplification due to execution on the

***contextOfUse*** element only

* + Flexibility of dossier[[3]](#footnote-4) granularity and grouping of documents
  + Referencing documents across applications
  + Re-use of documents

# CHANGE CONTROL RULES

Change requests need to be addressed to the relevant organisation, which is responsible for the standard or the implementation, based on:

* eCTD v4.0 is based on the HL7 Version 3 Regulated Product Submission (RPS) Message Standard Release 2 Normative, which was developed in the external Standards Development Organisation (SDO), Health Level Seven International (HL7) and various stakeholders, which includes members of ICH M8 and EU representatives. Changes of the RPS Standard need to be addressed according to rules [outlined at HL7.](http://www.hl7.org/events/harmonization/index.cfm)

* Changes to the ICH eCTD v4.0 IG and ICH Controlled Vocabularies remain the responsibility of the ICH M8 Expert Working Group & Implementation Working Group (ICH M8 EWG & IWG) and will follow the established [eCTD change control](http://www.ich.org/products/process-of-harmonisation.html) [process.](http://www.ich.org/products/process-of-harmonisation.html)
* In a situation where EU M1 IG needs to be changed, for example as a result of EU M1 content changes, changes to the regional requirements for applications that are outside the scope of the CTD, or identification of new functional requirements or experience of use of eCTD Module 1 gained by all parties, should be submitted to the [EMA Service Desk](https://support.ema.europa.eu/esc). All Change Requests and Questions can be submitted to <https://support.ema.europa.eu/esc> .

# ESSENTIAL COMPONENTS OF THE ECTD IN CONSIDERATION OF THE SPECIFIC REGIONAL EU REQUIREMENTS

The XML message provides the ability to describe the contents of the regulatory exchange and all information needed to process the exchange between the parties by using the following essential components:

|  |  |  |
| --- | --- | --- |
| **Component** | **Further information** | |
| **eCTD v4.0 EU M1 IG**  **(this document)** | **ICH eCTD 4.0 IG** |
| Object Identifier (OIDs) | - | Section 4.5.1 |
| Universal Unique Identifier (UUIDs) | - | Section 4.5.2 |
| Data Types | - | Section 4.6 |
| Files and Folders | SUBMISSION CONTENTS, FOLDER AND FILE STRUCTURE | Section 4.1 and  Section 11: Appendix 1 |
| Controlled Vocabulary | CONTROLLED VOCABULARIES | Section 4.2 and Section 6 |
| ICH eCTD v4.0 XML Schema | ECTD V4.0 XML SCHEMA | Section 4.3 and Section 7 |
| eCTD v4.0 XML Message | ECTD 4.0 XML MESSAGE | Section 9 |
| EU regional specific requirements for elements | EU REGIONAL SPECIFIC REQUIREMENTS FOR ELEMENTS |  |
| Validation Rules | XML MESSAGE VALIDATION RULES | Section 12: Appendix 2 |
| Forward Compatibility | COMPATIBILITY WITH AND REFERENCE TO PREVIOUS VERSIONS OF EU ECTD MODULE 1 | Section 8 |

The principles of creation and use of these components will be defined by

* ICH eCTD IG across regions (separate document[[4]](#footnote-5))
* EU Module1 IG regionally (this document)

Therefore, to compose a complete eCTD v4.0 compliant message, the user additionally needs to refer to the requisite documentation published by ICH[[5]](#footnote-6).

## Elements for regional use covered by EU Module 1 Implementation Guide

For EU Module 1 the following elements are required, and EU-specific business rules apply:

* ***application***
  + ***subject.reviewProcedure***
  + ***reference.applicationReference***
  + ***holder.applicant*** (different from the ICH IG)
  + ***informationRecipient.territorialAuthority***
* ***submission***
  + ***subject2.review***
    - ***subject1.manufacturedProduct***
    - ***subject2.productCategory***
  + ***subject3.mode***
  + ***subject5.submissionGroup***

### Elements not required for EU Module 1

For EU Module 1 the following elements are not required in addition to those which are excluded by ICH already:

* ***componentOf2.categoryEvent***
  + ***component.categoryEvent***
* ***submission***
  + ***subject2.review.holder.applicant***
  + ***subject4.regulatoryReviewTime***

***Note to Implementers:*** *If these elements and associated elements and attributes are included in the XML message, they will be ignored by the receiver.*

## Regional Business Processes Covered by EU Module 1 Implementation Guide

This document will address the following regional business processes:

* + - **Dossier Management/Submission Life Cycle** – includes rules for Submission Unit, Submission and Applications (see section 10.2 of this document).
    - **Grouped Submissions** (e.g. EU PSUR single assessment, grouped variations, work share procedures) – includes rules for sending Submission Units that will reference more than one submission component (see section 9.17 and [section](#_bookmark150) 10.3 of this document).
    - **Two-way Communication** – It is currently not foreseen that this feature will be implemented in the EU.

# SUBMISSION CONTENTS, FOLDER AND FILE STRUCTURE

Although the eCTD v4.0 specification does not require a specific folder and file structuring or naming convention, the following rules may provide a best practice

recommendation on practical aspects on storing the files locally.

## Submission Unit Content in eCTD v4.0 Messages

The Submission Unit consists of a *First Level Folder* (see Section 5.3), the *Second Level Folder* (see section 5.4), the eCTD v4.0 XML Message for that individual Submission Unit, named “*submissionunit.xml*”, the text file providing the checksum (sha256) of the submissionunit.xml file, named “*sha256.txt”*, the folder m1 (see section 5.6) and, as appropriate, m2 to m5.

***Notes:***

* + - The sender should not send the schema files – i.e. the util folder of previous versions of the eCTD is no longer required. The XML should reference the interaction schema being used.
    - All files included in these folders should be accounted for in the XML message.
    - Files previously sent do not need to be sent again.
    - It is possible to reference documents across applications (equivalent to the term dossier).

It is not the intent of the eCTDv4.0 Implementation Guide to introduce content related business rules which may be used for business validation after structured authoring of content has been introduced and may offer additional validation rules.

## Naming Conventions

The naming conventions for files and folders for EU Module 1 will be replaced by keywords using controlled vocabularies (see section 6) at the level of ***submissionUnit.component.contextOfUse***, which is also required for selective display of information. This also includes language and country information (see also Section 10.1.3). Additional guidance is outlined in the ICH eCTD IG section 5.2.

### Allowable Characters

There are no additional requirements other than those outlined in the ICH eCTD IG.

### Length of Names and the Path

There are no additional requirements other than those outlined in the ICH eCTD IG.

## First Level Folder Naming Convention

The first level folder structure is required to identify the content within it e.g. when on portable electronic media or after extracting compressed content from a container. The name of the folder should be the application number allocated by the EMA or NCA. Any punctuation (such as hyphens, slashes, underscore) should be removed from this name and the text should be in lower case. For example:

* + - **de2087** or **fr3456** in case of the MR/DC procedure i.e. DE/H/2087/001/MR or FR/H/3456/001-005/DC respectively,
    - **de2131577** in case of a national German procedure,
    - **ema000123** in case of the Centralised procedure EMEA/H/C/000123 or EMEA/H/C/000123/II/14 (if known).

In the case of **grouping (g) or worksharing (ws)** regulatory activities, including PSUR submission and single assessment procedures, several Submission Unit XML files related to each one-to-one application will be submitted together in a ZIP file. The XML files will be extracted and stored as usual. The PDF’s will be submitted once and reused in the applications.

The ZIP file should be named with the grouping, workshare or PSUSA number as shown below:

* + - **de0001g** or **fr0019g** in the case of grouping, where DE or FR are the first or nineteenth grouping, respectively.
    - **es0002ws** or **fi0005ws** in the case of worksharing where ES or FI are the RMS, and the second or fifth worksharing for a national procedure submission across some member states.
    - **ema0011g or ema0009ws** in the case of a centrally authorised product being involved in grouping or worksharing, respectively.
    - **PSUSA00002172** in case of an EU PSUR Single Assessment Procedure, e.g. PSUSA/00002172/2015 (pending EMA decision if the PSUSA will be added in the Submission Mode RMS list, next to single, grouping, worksharing)

Regardless of the naming convention of the root folder, the eCTD tool should independently manage the storing of the sequences at the correct location.

For further details on handling groupings and worksharing see Section 10.3.1

## Second Level Folder Naming Requirements

The second level folder name is the sequence number. The sequence number is a positive whole number between “1” and “999999”. The first submission in eCTD v4.0 format will have sequence number “1”. This allows storing incoming sequences on the file share in a simple way.

## Pathname Conventions and Best Practices

There are no additional requirements other than those outlined in the ICH eCTD IG.

## Folder Hierarchy

Module 1 will be a single folder with no additional folder structure. Country, dosage, and strength information will be defined using keywords for Controlled Vocabulary and ContextofUse rather than folder structure. For language attributes see section 10.1.3*.*

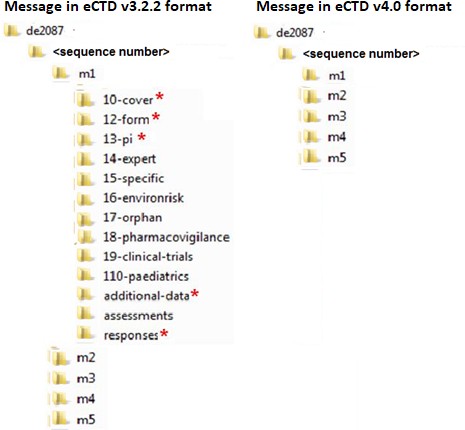


Figure Folder Hierarchy of Module 1 Screenshot

## File Formats

The following file formats are acceptable for the EU Module 1:

  
 *Note:*  
*The list of acceptable file formats is under review, and it will be confirmed in the final version of the EU Implementation Guide**. The list will be included as a chapter in the Implementation Guide, or in a separate annex.*

Table : Acceptable file formats for Module1

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **File Type** | **File Format** | **Format Name** | **Expected**  **Location(s) in eCTD** | **Permissible Uses / Comments** |
| *Documents* |  |  |  |  |
|  | .pdf\* | Portable Document Format | M1 – M5 | PDF/A-1, PDF/A-2, 1.4, 1.5, 1.6, 1.7 |
|  | .txt | Text file | M5 | Datasets |
|  | .xlsx | Microsoft Excel Open XML document | M5 | Datasets |
| *Images* |  |  |  |  |
|  | .bmp | Bitmap Graphics | M1.3.2, M1.3.3 | Mock-Ups / Specimens |
|  | .gif | Graphics Interchange Format | M1.3.2, M1.3.3 | Mock-Ups / Specimens |
|  | .jpg, .jpeg | Joint Photographic Experts Group | M1.3.2, M1.3.3 | Mock-Ups / Specimens |
|  | .png | Portable Network  Graphics | M1.3.2, M1.3.3 | Mock-Ups / Specimens |
| *Audio/Video* |  |  |  |  |
|  | .avi | Audio Video Interleaved | M1.3, M2, M5 | Labelling, M2 summaries & overviews, CSRs |
|  | .mpeg | Moving Picture Experts Group | M1.3, M2, M5 | Labelling, M2 summaries & overviews, CSRs |
|  | .mp4 | MPEG-4 Part 14 | M1.3, M2, M5 | Labelling, M2 summaries & overviews, CSRs |
|  | .wmv | Windows Media Video | M1.3, M2, M5 | Labelling, M2 summaries & overviews, CSRs |
| *Coding Language* |  |  |  |  |
|  | .xml\*\* | Extensible Markup Language | M1.2, M1.3, M4, M5 | eAF, Labelling, Datasets, ePI |
|  | .xsd | XML Schema Definition | M4, M5 | Clinical (ISS) datasets |
|  | .xsl | Extensible Stylesheet Language | M1, M4 - M5 | \util\style folder, data |
| Data |  |  |  |  |
|  | .csv | Comma Separated Values file | M5.3.3.5 | Population PK Studies |
|  | .svg | Scalable Vector Graphics | M3 – M5 |  |
|  | .xpt | SAS Transport file | M3 – M5 |  |

\* Additional details on PDF and PDF/A formats can be found in [ICH M2 recommendations.](http://www.ich.org/products/electronic-standards.html)

\*\* In line with the general principles of the ICH eCTD Implementation Guide, it is intended that XML will eventually become the *de facto* submission format for administrative forms (because they contain structured data, and a long-term goal of this development is the normalisation of data in Module 1).

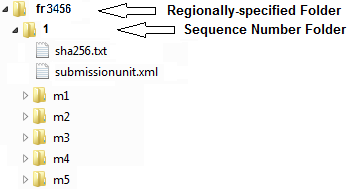
Respective stylesheets need to be accessible at a public domain.

## Checksums

The purpose of the checksum is as follows:

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

The checksum of the submissionunit.xml needs to be provided as a separate text file, named sha256.txt and will be in the sequence number folder:



**Figure 2: Submission Unit Folder Structure**

The value will be checked against the submissionunit.xml file submitted. In case the value is not matching, the message will be rejected.

# CONTROLLED VOCABULARIES

As mentioned in the ICH implementation guide, controlled vocabularies are one of the essential components of the eCTD v4.0, which enable interoperability – i.e., clear, unambiguous communications between systems sending and receiving XML messages. For the XML elements that have coded values, a controlled vocabulary will be required to indicate the value of the concept. Each code has a code system. The code system may be managed by ICH, Region, or the Applicant. The specific assignment of code system values can be found in the detailed description of OIDs and controlled vocabularies.

Controlled vocabularies are defined external to the message; a code is used as the identifier to convert the code value into the meaningful terms that will be used in any system that implements the viewing of the information sent in the XML message.

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

The information in the following sub-sections will outline the controlled vocabulary used in composing an eCTD v4.0 message. There are several different authoritative sources for the controlled vocabularies, and as such they are categorised below by the organisation that controls the content. The ICH eCTD v4.0 specific terminologies, i.e. the controlled vocabulary determined by ICH, are stated in the ICH Implementation Guide.

The EU has its own organisation root OID registered on the HL7 registry:

{joint-iso-itu-t(2) country(16) us(840) organisation(1) hl7(113883) externalUseRoots(3) ich-estri(989) regional-specialised(5) sub-reg(1) eu(1)} or being read as:

2.16.840.1.113883.3.989.5.1.1(optional child OIDs to be added),

which is extended to assign a specified OID for dossier management (“6”), where the EU M1 IG (“1”) is being part of and which relates to its first final version (“1”) for implementation use:

2.16.840.1.113883.3.989.5.1.1.6.1.1(EU M1 IG v1.0)

A different OID assigned to the EMA is valid for controlled vocabularies related to the Referential Management System as part of SPOR data services[[6]](#footnote-7). The relevant controlled vocabularies are provided in the Implementation Package in genericode machine readable format (“2” and its first version (“1”):

2.16.840.1.113883.3.989.5.1.1.6.2.1(EU M1 Controlled vocabularies v1.0)

***Notes to Implementers:***

* *The controlled vocabulary required 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 Competent Authorities.*
* *For implementation, the controlled vocabulary will be provided using on OID assigned specifically. All EU regionally required controlled terms are also available at:* [*https://spor.ema.europa.eu/sporwi/*](https://spor.ema.europa.eu/sporwi/)*.*

## Keywords and Controlled Vocabularies for EU Purpose

Keywords need to be used to support a reader friendly presentation of content within the same context of use, either by sender defined ***keywordDefinition*** or using a controlled vocabulary, i.e. for document type, language, country. In EU Module 1,

documents in the context of use for “10-cover”, 12-form”, “13-pi”, “additional-data”, and “responses”, the use of keywords for country code is required. Depending on the product, additional sender defined keywords can be used to specify the pharmaceutical form or strength for which a product information text is dedicated. These sender-defined keywords should be used for Module 3 purpose at the same time. However, dedicated rules cannot be stated here as they will depend on individual products or sender specific rules to be applied across their product portfolio. It is not foreseen to re-submit ***keywordDefinition*** values in each sequence. However, sender defined keywords can be modified but will be executed then for all applications making use of them (see section 9.24).

***Note to Implementers:*** *The previously required language folder in “13-pi” will be replaced by documentLanguage.code (see section* 9.23*)****.***

The controlled vocabularies specified for the EU Module 1 part of the eCTD v4.0 message are described below including terminology and location for obtaining detailed information[[7]](#footnote-8).Currently no versioning is foreseen for terms to be used for eCTD v4.0. A new version of the CV set will have its own OID. This will guarantee that the correct version of the term IDs can be identified. Updates should not be executed automatically. However, the assumption is made of always displaying the most recent version of a term of which the ID of the code system is inserted into the XML file. In case, the code system ID is provided correctly, the software can download / integrate / have to look-up what the current display value will be. The display value will then always be the most recent expression.

***Note to Implementers:*** *For convenience, the displayName values of several codes are provided in the XML snippets. However, the display name is not required for processing of a submissionunit.xml file. Instead, any displayName value will be ignored as it should be retrieved from the respective codeSystem as described in the section above.*

Table : Controlled Vocabularies for EU purpose

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Referenced Controlled Term List in ICH IG v1.3 for eCTD v4.0 being used for EU submissions** | **EU List Name** | **Purpose** | **Source in RMS OID extension** | **Comment** |
| Application Codes | **EU Application Code - Legal Basis** | This list describes the legal basis for a Marketing Authorisation application. | <https://spor.ema.europa.eu/rmswi/#/lists/100000116045/terms>    2.16.840.1.113883.3.6905.2 |  |
| Application Reference Reason Codes | **EU Application Reference Reason** | Reasons why a reference to an already authorised medicinal product is used, e.g. in the case of a generic product. | <https://spor.ema.europa.eu/rmswi/#/lists/100000154440/terms>  2.16.840.1.113883.3.6905.3 |  |
| Contact Party Codes | **Contact Party Role** | Details of the legally defined contact person(s) of the sponsor, i.e. the roles,  which a contact person of the sponsor can have by submitting an eCTD. | <https://spor.ema.europa.eu/rmswi/#/lists/100000154441/terms>  2.16.840.1.113883.3.6905.6 |  |
| Context of Use Codes: Specifies the code set to represent the headings found in the CTD structure that are required for EU Module 1). | **EU eCTD Context of Use** | Examples of enhancement features and the re-use of data are in the context of use which will allow one piece of data to be used across many applications, avoiding the need for duplication of data elements. | <https://spor.ema.europa.eu/rmswi/#/lists/100000155719/terms>  2.16.840.1.113883.3.6905.7 |  |
| Keyword Codes: Specifies the keyword types that have controlled vocabulary | **Product Information Document Type** | Type of keyword that is applied to a product information document. or document types, where the language needs to be specified. The Controlled Term List contains the types of product information documents, which are part of the eCTD Module 1.3.1. | <https://spor.ema.europa.eu/rmswi/#/lists/100000155531/terms>  2.16.840.1.113883.3.6905.14 |  |
|  | **Document Type Codes** | The Controlled Term List contains the types of any other document types. | <https://spor.ema.europa.eu/rmswi/#/lists/100000155531/terms>    2.16.840.1.113883.3.6905.20 |  |
|  | **Language** | Keyword codes language keywords as defined by the ContextOfUse controlled vocabulary for EU Module 1 | Will apply to document type (see Document Type Codes), language, country ([Section 6.3](https://usc-word-edit.officeapps.live.com/we/wordeditorframe.aspx?ui=es%2DES&rs=en%2DUS&wopisrc=https%3A%2F%2Fpfizer.sharepoint.com%2Fsites%2FeCTDv4.0ImplementationTeam%2F_vti_bin%2Fwopi.ashx%2Ffiles%2F469218e7177a4be28e68dcda098b2744&wdenableroaming=1&mscc=1&hid=8401BFA0-B0D7-3000-BE33-44F7915A2EC4&wdorigin=Other&jsapi=1&jsapiver=v1&newsession=1&corrid=2f411460-ab18-48f6-b32e-9cda6cf6ac57&usid=2f411460-ab18-48f6-b32e-9cda6cf6ac57&sftc=1&cac=1&mtf=1&sfp=1&instantedit=1&wopicomplete=1&wdredirectionreason=Unified_SingleFlush&rct=Normal&ctp=LeastProtected#_Controlled_Vocabulary_specified))  <https://spor.ema.europa.eu/rmswi/lists/100000072057/terms>  2.16.840.1.113883.3.989.5.1.2.2.1.101.1  (constrained for EU purposes) | Language Code restricted to EEA |
|  | **Manufactured Product Form** | Type of the pharmaceutical product under review based on the pharmaceutical form (single and combined).  The same will be used for keyword ‘pharmaceutical form’ as outline in the ContextOfUse controlled vocabulary for EU Module 1 | <https://spor.ema.europa.eu/rmswi/#/lists/200000000004/terms>  <https://spor.ema.europa.eu/rmswi/#/lists/200000000006/terms>  2.16.840.1.113883.3.6905.12 |  |
| Ingredient Role Codes | **EU Ingredient Role** | Role of each of the ingredients in the composition of a medicinal product. | <https://spor.ema.europa.eu/rmswi/#/lists/100000072050/terms>  2.16.840.1.113883.3.6905.11 |  |
| Mode Codes | **Submission Mode** | Indicates whether the regulatory activity will be handled as a group, single or work shared manner. as well as for PSUR Single Assessment procedure submissions.. | <https://spor.ema.europa.eu/rmswi/#/lists/100000155553/terms>  2.16.840.1.113883.3.6905.16 |  |
| Place Codes | **EU Place Codes** | Used to name the territorial area for which the competent authority’s decision will apply to.  Competent Authorities responsible for Medicinal Product authorisation in the EU and the EEA, including name of the country. In the case of eCTD, the usage is restricted to Competent Authorities responsible for human medicinal products | <https://spor.ema.europa.eu/rmswi/#/lists/100000160680/terms>  2.16.840.1.113883.3.6905.18 |  |
| Product Category Codes | **Product Category** | This Controlled Term List is used to indicate the overall category of a human medicinal product based on its active  ingredients, e.g. chemical, herbal or biotech product. | <https://spor.ema.europa.eu/rmswi/#/lists/100000155526/terms>  2.16.840.1.113883.3.6905.13 |  |
| EU Regulatory Authorisation/Registration Procedure Type Codes | **Procedure Type Codes** | Type of regulatory authorisation procedure in the European Union. | <https://spor.ema.europa.eu/rmswi/#/lists/100000154442/terms>  2.16.840.1.113883.3.6905.9 |  |
| Submission Codes | **Application Submission Type** | Type of regulatory activity constituted by one or several Submission Units and referring to at least one application. | <https://spor.ema.europa.eu/rmswi/#/lists/100000155688/terms>  2.16.840.1.113883.3.6905.4 |  |
| Submission Unit Codes | **Applicant’s Submission Unit Type** | Types of content of Submission Unit items to be provided by an applicant | <https://spor.ema.europa.eu/rmswi/#/lists/100000155046/terms>  2.16.840.1.113883.3.6905.1 |  |
| Territorial Codes | **Country Codes** | Used to name the territorial area for which the competent authority’s decision will apply to (constrained to EU countries). | <https://spor.ema.europa.eu/rmswi/#/lists/100000000002/terms>  2.16.840.1.113883.3.6905.10 |  |

****

***Note to Implementers****: The following lists will not be provided as a genericode or spreadsheet, as they are dynamic and the publication of the new versions of the lists would delay the use of these terms; instead, the codes can be found in the pages below, through the user interface or API, if available:*

***Substances (OID:*** tbd***)****:* [SPOR Web UI (europa.eu)](https://spor.ema.europa.eu/smswi/#/)

***Organisations (OID:*** tbd***)****:* [OMS Web UI (europa.eu)](https://spor.ema.europa.eu/omswi/#/)

*Further details, including on the retrieval of the* ***Products (OID:*** tbd***)****, and on how to connect will be provided at a later date.*

*All the IDs will be validated upon receiving them.*

## Controlled Vocabulary specified by HL7

The controlled vocabularies specified by Health Level 7 (HL7) will apply for EU Module 1 in the same way as for Modules 2 to 5, see ICH eCTD IG for details.

## Controlled Vocabulary specified by ISO

The controlled vocabulary specified by other organisations (i.e. not managed by ICH, Region or HL7) are provided below, denoting the responsible organisation, a brief description of the terminology and location for obtaining detailed information.

* + - **International Organisation for Standardization (ISO) - Two-Letter Language Code**: This is a two-letter code that is specified for the language as specified in the ISO 639.1 standard. This vocabulary is used to define the ***text@language*** attribute. For EU Module 1 purposes a constrained list will be used (see [SPOR RMS](https://spor.ema.europa.eu/v1/lists/100000072057)).
    - **ISO Country Code – Two-letter Country Code:** This is the country code that is specified in the ISO 3166-1 standard. For EU Module 1 purposes a constrained list will be provided by the [SPOR RMS](https://spor.ema.europa.eu/v1/lists/100000000002).
    - **ISO 11238 (current version) Health informatics – Identification of Medicinal Products – Data elements and structures for the unique identification and exchange of regulated information on substances**. Based on this standard a specific data base will be developed including a generic API. It seems to be possible that in future time several of the metadata can be replaced by referencing the product ID once established in the European product data basis.

## Maintenance of Controlled Vocabularies

International vocabulary harmonisation for eCTD v4.0 is out of scope for the initial release of eCTD v4.0 and implementers may use existing vocabularies that are unique to their message exchange requirements between parties.

Maintenance of Controlled Vocabularies from outside the EU region will be handled by the M2 Working Group. All other controlled vocabularies will be handled by RMS of the SPOR Web UI[[8]](#footnote-9) for EU Module 1 use.

# ECTD V4.0 XML SCHEMA

There are no principles deviating from the ICH eCTD IG for using the EU part of the XML schema.

# ECTD 4.0 XML MESSAGE

There are no principles deviating from the ICH Implementation Guide for creating the EU part of the XML message. Especially regarding to the header of the message the same elements/attributes apply as outlined in the ICH eCTD IG. In addition, the conceptual model is identical to what is described in the ICH IG.

Nevertheless, additional regional specific requirements need to be considered for other elements/attributes as outlined below.

***Note to Implementers:*** The ***value*** elements should be provided in the XML alongside the ***codeSystem*** and ***code***. However, the display name provided by the ***value*** element will not be validated and should not be displayed by tools. The ***codeSystem*** and ***code*** values will be validated and the associated name value from the Code System itself should be displayed in tools instead.

All information in this section is organised in order to enable the eCTD v4.0 XML components to appear within the schema. Elements /attributes that are not required in the EU are indicated as such in table 3, below.

***Note to Implementers:*** *Elements, associated elements and attributes that are not required in the EU but are included in the XML message will be ignored by the receiver.*

## Example for the header as to be used in the EU region

|  |
| --- |
| <PORP\_IN000001UV ITSVersion="XML\_1.0" xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance" xsi:schemaLocation="urn:hl7-org:v3 PORP\_IN000001UV.xsd">  <id/>  <creationTime/>  These elements should be represented with self-closing tags as shown here.  <interactionId/>  <processingCode/>  <processingModeCode/>  <acceptAckCode/>  <receiver>  <device classCode="DEV" determinerCode="INSTANCE">  <id>  <item root="" identifierName=""/>  </id>  </device>  </receiver>  <sender>  <device classCode="DEV" determinerCode="INSTANCE">  <id/>  </device>  </sender> |

* ***ITSVersion*** must provide the value of "XML\_1.0"
* ***xmlns*** must have the value "urn:hl7-org:v3"
* ***xmlns:xsi*** must have the value "http://www.w3.org/2001/XMLSchema-instance"
* ***xsi:schemaLocation*** must reference the current interaction schema file i.e., xsi:schemaLocation=
* ***receiver@typeCode*** has a fixed value of "RCV" and it does not need to be included in the message.
* ***receiver.device@classCode*** must have a value of "DEV"
* ***receiver.device@determinerCode*** must have a value of "INSTANCE"
* Include two ***id.item*** elements with the following information:
  + ***receiver.device.id.item@root*** should indicate the OID of the ICH eCTD v4.0 Implementation Guide or the Regional/Module 1 Implementation Guide used to create the message.
  + ***receiver.device.id.item@identifierName*** should indicate the version name of the ICH eCTD v4.0 Implementation Guide or the Regional/Module 1 Implementation Guide used to create the message. This value can be used to indicate the version number of the IG, but will not be used by the Regulatory Authority.
* ***sender@typeCode*** has a fixed value of "SND" and it does not need to be included in the message
* ***sender.device@classCode*** must have a value of "DEV"
* ***sender.device@determinerCode*** must have a value of "INSTANCE"

### XML Sample

<id/>

<creationTime/>

<interactionId/>control

<processingCode/>

<processingModeCode/>

<acceptAckCode/>

<receiver>

<device classCode="DEV" determinerCode="INSTANCE">

<id>

<item root="2.16.840.1.113883.3.989.2.2.1.11.4" identifierName="ICH eCTD v4.0 IG v1.5"/>

<item root="2.16.840.1.113883.3.989.5.1.1.6.1.1" identifierName="EU M1 IG v1.0"/>

</id>

</device>

</receiver>

<sender>

<device classCode="DEV" determinerCode="INSTANCE">

<id/>

</device>

</sender>

## Structure of the eCTD v4.0 payload message adapted to EU regional purposes

The following tables provide the structure of the payload message and indicate the relevant section for detailed explanations.

Table : XML Structure

|  |
| --- |
| **XML Structure** |
| The eCTD v4.0 begins at the ***controlActProcess*** of the payload XML message related to Module 1 content. |
| <controlActProcess classCode="ACTN" moodCode="EVN">  <subject typeCode="SUBJ"> |
| The ***submissionUnit*** element contains the following Context of Use elements and their attributes:   * ***component.contextOfUse***   + ***primaryInformationRecipient.TerritorialAuthority***   + ***replacementOf.relatedContextOfUse***   + ***derivedFrom.documentReference***   + ***subjectOf.submissionReference***   + ***referencedBy.keyword*** |
| <submissionUnit>  <id/>  ***submissionUnit (Section***  9.1***)***  as a supplement to the ICH eCTD IG  <code/>  <title/>  <statusCode/>  ***priorityNumber (Section*** 9.2 ***)***  as a supplement to the ICH eCTD IG  <component>  <priorityNumber value=""/>  <contextOfUse>  ***contextOfUse (Section*** 9.3*Error! Reference source not found.****)*** as a supplement to the ICH eCTD IG  <id/>  <code/>  <statusCode/>  <primaryInformationRecipient>  <territorialAuthority>  ***primaryInformationRecipient.territorialAuthority (Section*** 9.4***)***  specific for EU Module 1 IG  <governingAuthority>  <id/>  <name/>  </governingAuthority>  </territorialAuthority>  </primaryInformationRecipient>  <replacementOf typeCode="RPLC">  <relatedContextOfUse>  ***replacementOf.relatedContextOfUse (Section*** 9.5***)***  <id/>  </relatedContextOfUse>  </replacementOf>  <derivedFrom>  <documentReference>  ***derivedFrom.documentReference (Section*** 9.6***)***  <id/>  </documentReference>  </derivedFrom>  <subjectOf>  ***submissionReference (Section*** 9.7***)***  specific for EU Module 1 IG  <submissionReference>  <id><item/></id>  </submissionReference>  ***keyword (Section*** 9.8***)***  as a supplement to the ICH eCTD IG and specific for EU Module 1 IG  </subjectOf>  <referencedBy typeCode="REFR">  <keyword>  <code/>  </keyword>  </referencedBy>  </contextOfUse>  </component> |
| This section of the XML relates to specifying the ***submission*** element. The following elements may follow the Submission:   * ***sequenceNumber*** (included as an element of the relationship between ***submissionUnit*** and ***submission*** elements) * ***callBackContact.contactParty*** * ***subject1.regulatoryStatus (excluded)*** * ***subject2.review***    + ***subject1.manufacturedProduct***   + ***holder.applicant***   + ***author.territorialAuthority***   + ***subject2.productCategory*** * ***subject3.mode*** * ***subject4.regulatoryReviewTime (excluded)*** * ***subject5.submissionGroup*** |
| <componentOf1>  ***sequenceNumber.submission*** ***(Section*** 9.9***)***  <sequenceNumber/>  <submission>  ***Submission (Section*** 9.10***)***  <id/>  <code/>  <callBackContact>  <contactParty>  <id/>  <code/>  <statusCode/>  ***callBackContact (Section*** 9.11***)***  Specific for EU Module 1 IG  <contactPerson>  <name/>  <asAgent>  <representedOrganization>  <id/>  <name/>  </representedOrganization>  </asAgent>  </contactPerson>  </contactParty>  </callBackContact>  <subject1>  ***regulatoryStatus*** – Excluded due to omission by ICH IG  <regulatoryStatus>  <code/>  </regulatoryStatus>  </subject1> |
| <subject2>  <review>  ***Review (Section*** 9.12***)***  Specific for EU Module 1 IG  <id/>  <statusCode/>  <effectiveTime/>  ***manufacturedProduct (Section*** 9.13***)***  Specific for EU Module 1 IG  <subject1>  <manufacturedProduct>  <manufacturedProduct>  <name/>  </manufacturedProduct>  ***review.holder*** – Refer to Regional/Module 1 Implementation Guides  </manufacturedProduct>  </subject1>  <holder>  <applicant/>  </holder>  ***review.territorialAuthority (Section )*** Specific for EU Module 1 IG  <author>  <territorialAuthority/>  </author>  <subject2>  ***productCategory (Section*** 9.15***)***  Specific for EU Module 1 IG  <productCategory>  <code/>  </productCategory>  </subject2>  <subject3>  <regulatoryStatus>  ***regulatoryStatus*** – not being used in the EU in case of applicant’s submission  <code/>  </regulatoryStatus>  </subject3>  </review>  </subject2>  ***mode (Section*** 9.16***)***  Specific for EU Module 1 IG  <subject3>  <mode>  <code/>  </mode>  </subject3>  <subject4>  ***regulatoryReviewTime*** – excluded due to omission by ICH IG  <regulatoryReviewTime>  <code/>  </regulatoryReviewTime>  </subject4>  <subject5>  ***submissionGroup (Section*** 9.17***)***  Specific for EU Module 1 IG  <submissionGroup>  <id/>  </submissionGroup>  </subject5> |
| **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.keywordDefinition (excluded)*** |
| <componentOf>  ***application (Section*** 9.18  as a Supplement to the ICH eCTD IG and Specific for EU Module 1 IG  <application>  <id>  <item/>  </id>  <code/>  <holder>  <applicant>  ***holder.applicant (Section*** 9.19***)***  Specific for EU Module 1 IG  <sponsorOrganization>  <id><item></item></id>  <name></name>  </sponsorOrganization>  </applicant>  </holder>  <informationRecipient>  <territorialAuthority>  ***informationRecipient.territorialAuthority (Section*** 9.20***)***  Specific for EU Module 1 IG  <governingAuthority>  <id/>  <name/>  </governingAuthority>  </territorialAuthority>  </informationRecipient>  <subject>  ***reviewProcedure (Section*** 9.21***)***  Specific for EU Module 1 IG  <reviewProcedure>  <code/>  </reviewProcedure>  </subject>  <reference>  ***applicationReference (Section*** 9.22***)***  Specific for EU Module 1 IG  <applicationReference>  <id/>  </applicationReference>  </reference> |
| <component>  <document>  <id/>  ***document (Section*** 9.23*Error! Reference source not found.)*  <title/>  <text integrityCheckAlgorithm="" mediaType="" language="">  <reference/>  <integrityCheck/>  ***keyword*** – Excluded due to omission by ICH IG  </text>  <referencedBy typeCode="REFR">  <keyword>  <code/>  </keyword>  </referencedBy>  </document>  </component>  <referencedBy>  <keywordDefinition>  <code/>  <statusCode/>  ***keywordDefinition (Section*** 9.24***)***  Specific for EU Module 1 IG  <value>  <item code="" codeSystem="">  <displayName/>  </item>  </value>  </keywordDefinition>  </referencedBy>  </application>  </componentOf>  </submission>  </componentOf1> |
| 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***). |
| <componentOf2>  <categoryEvent>  ***subject.categoryEvent*** Not required  <code/>  <component>  <categoryEvent>  <code/>  </categoryEvent>  </component>  </categoryEvent>  </componentOf2>  </submissionUnit>  </subject>  </controlActProcess>  </PORP\_IN000001UV> |

# EU REGIONAL SPECIFIC REQUIREMENTS FOR ELEMENTS

## Submission Unit

The Submission Unit is a collection of documents provided to the Regulatory Authority. A Submission Unit always relates to a regulatory activity specified by the submission that is related to a specified application.

Only one Submission Unit can be sent at a time related to one regulatory activity and application. The Submission Unit may be in response to one or more lists of questions from a Regulatory Authority, with respect to the specified application and Submission Unit.

Whenever a Submission Unit needs to be withdrawn by the applicant, a new message needs to be sent providing the new status code “suspended” of that previously submitted unit. In this case, content references are not required as the status code of document elements will not change, and CoU elements are not affected. In consequence, the documents will no longer be displayed for the application and Submission Unit that was withdrawn, but they can still be used and will be displayed when referenced by other applications.

### Location in XML

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

* + - * ***controlActProcess*** >> ***subject*** >> ***submissionUnit***

Refer to Table 4: XML Structure for the XML representation.

### XML details

There are no additional requirements other than those outlined in the ICH eCTD IG.

***XML Elements***

Tables with a complete set of XML elements and attributes required for the ***SubmissionUnit*** element are provided in the ICH eCTD IG and will not be repeated in this document. No additional requirements apply for EU M1.

***XML Sample: Submission Unit***

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

<subject typeCode="**SUBJ**">

<submissionUnit>

<id root="**c503dce7-d628-42c1-861a-ab738afe739d**"/>

<code code="**100000155047**" codeSystem="2.16.840.1.113883.3.6905.1"/>

<!-- Initial submission to start a regulatory activity -->

<title value="**Initial**"/>

<statusCode code="**active**"/>  
<!--*[Additional information may appear after the addition of the* ***statusCode*** *(if one exists), otherwise this will come after the* ***title*** *or* ***code elements.*** *For example, depending on the type of Submission Unit the additional elements may be available to select from the Submission Unit* ***component*** *or* ***componentOf1*** elements.-->

<componentOf1>

<sequenceNumber value="**1**"/>

<submission>

<!--*Additional information will follow for the* ***submission*** *elements.* -->

<componentOf>

<application>

<!-- *Additional information appears for the* ***application*** *element.* -->

</application>

</componentOf>

</submission>

</componentOf1>

</submissionUnit>

</subject>

*Note: If a status code is provided, a submissionUnit.Code must be provided as well. The status code values are ‘active’ or ‘suspended’.*

## Priority Number

There are no additional requirements other than those outlined in the ICH eCTD IG.

*Note: The life cycle will be executed by inserting a new* ***contextOfUse*** *element including the respective combination of keywords and by assigning the appropriate priority number. All life cycle considerations outlined in the ICH eCTD IG will apply to EU Module 1 in the same manner.*

## Context of Use

The Context of Use (CoU) provides a linkage between the table of contents heading of the CTD and the referenced document that is associated to that heading including a label for a short instructive information on the document referenced (document label). There are no additional technical requirements other than those outlined in the ICH eCTD IG. In the sections below, the examples will be provided for EU Module 1.

*Note: The life cycle will be executed by inserting a new* ***contextOfUse*** *element including the respective combination of keywords and by assigning the appropriate priority number. All life cycle considerations outlined in the ICH eCTD IG will apply to EU Module 1 in the same manner.*

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>component>> contextOfUse***

Refer to Table 4: XML Structure for the XML representation.

### XML Details

There are no additional requirements other than those outlined in the ICH eCTD IG. However, as a relevant difference in comparison to eCTD v3.2.2 for product information texts the type of document will be defined by a controlled vocabulary list of document types (see section 6.1) and is stated as keyword at CoU. The dedicated territory, that the product information text is valid for, will be managed in the same way. Finally, pharmaceutical form and strength will be added as sender defined keywords to allow a proper ordering. There are no keywords possible to be assigned at ***document*** element.

### Terminology

The Context of Use codes will be provided by EU-specific controlled vocabularies (see section 6.1).

The desired status codes will be used in line with ICH eCTD IG definitions.

## Territorial Authority (as primary information recipient related to contextofUse)

* The optional element ***primaryInformationRecipient*** will provide names of ***territorialAuthority.governingAuthority*** in case a single ***contextOfUse*** element is dedicated to one agency separately. For Centralised procedures and in cases the Submission Unit contains documents for just one Concerned Member State, this means the element can be ignored as all documents will be relevant for all recipients of the message. In case of DCP or MRP, e.g. France may be named by using the ***primaryInformationRecipient*** element to restrict the display of the fee payment notification from ANSM to France.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>component>> contextOfUse>>primaryInformationRecipient>>territorialAuthority***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***territorialAuthority*** element in case it is provided, and any special instructions.

*The* ***classCode*** *is fixed to “TERR”. This value is not required in the XML message.*

***territorrialAuthority.governingAuthority***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinalit y** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***id*** |  | [1..1] |  | This is a container element for a reference to the name of the governing authority. |
| ***name.part*** |  | [1..\*] |  | This is the container element of the following attributes by which the name of the regulating authority is  provided. |
|  | ***Code*** | [1..1] | Alpha Numeric  e.g., 100000160772 | The ***code*** element will provide the unique identifier of the authority. |
|  | ***codeSystem*** | [1..1] | Valid OID or UUID  100000160680 | This is the ***codeSystem*** attribute that is a unique identifier for the controlled vocabulary system.  *This should be the OID or*  *UUID registered for the code system.* |
|  | ***Value*** | [0..1] | Alpha Numeric  e.g., DE-BfArM | The ***name*** element will display the name of the authority. |
| ***Conformance*** | The ***id*** element is required. | | | |
| ***Business Rules*** | This element provides the referencing point for the competent agency receiving the ***contextOfUse*** element as a primary recipient, e.g. the payment  notification of the French agency for France | | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinalit y** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id@identifierName*** * ***id@scope*** * ***id@reliability*** * ***id@displayable*** | | | |

***XML sample***

The sample covers elements described in section 9.1 to 9.8, except submission reference.

<submissionUnit>

<!-- ========================================================================-->

<!-- This is the root attribute that uniquely identifies the submission -->

<!-- The Submission Unit code is provided to indicate the type of submission unit -->

<!-- being submitted. Only one SubmissionUnit element can exist for a message -->

<!-- Note: All submissions referenced in the message will have the same submissionUnit code value.-->

<!-- ========================================================================-->

<id root="**65558ad6-eaa5-4f83-915b-57b4fb20a3f3**"/>

<!-- ========================================================================-->

<!-- Submission Unit must have a valid code value -->

<!-- Submission Unit Code System value is required -->

<!-- Submission Unit code must have a valid OID for the Code System value. -->

<!-- ========================================================================-->

<code code="**100000155047**" codeSystem="2.16.840.1.113883.3.6905.1"/>

<!-- ========================================================================-->

<!-- Initial submission to start a regulatory activity -->

<!-- displayName value="**initial** may be retrieved from the code list as indicated. -->

<!-- =========================================================================->

<title value="**Initial**"/>

<!-- ========================================================================-->

<!-- The Submission Unit status code requires the code attribute "active" -->

<!-- ========================================================================-->

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

<component>

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

<contextOfUse>

<!-- =======================================================================-->

<!-- Context of Use id root must be a unique identifier -->

<!-- =======================================================================-->

<id root="**ba7fb4f1-7305-4a67-8877-393e8d6fd343**"/>

<!-- ======================================================================->

<!-- CTD Heading -->

<!-- 100000164029 is the TermID for Cover Letter in RMS -->

<!-- =====================================================================-->

<code code="**100000164029**" codeSystem="2.16.840.1.113883.3.6905.7"/>

<!-- =======================================================================-->

<!-- ***displayName value***="**../m1/form-appendix5-12** may be retrieved from the -->

<!-- code list. Therefore, it must not be stated in the message. Instead, the ***originalText value***-->

<!-- element can be used to display a short instructive document label. This element is optional.-->

<!-- ========================================================================-->

<originalText value="**../m1 /form-appendix5-12**"/>

<!-- ==================================================================-->

<!-- ***ContextOfUse.statusCode***.value is required and can only be "active" or "suspended" --><!-- ===================================================================-->

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

<primaryInformationRecipient>

<territorialAuthority>

<governingAuthority>

<!-- =====================================================================>

<!-- TermID=100000160631 for FR-ANSM in RMS (Referentials Management Services)-->

<!-- =====================================================================>

<id root="**3ee89f8c-7543-4b7f-868e-c1bd3042c024**"/>

<code code="**100000160631**" codeSystem="2.16.840.1.113883.3.6905.10"/>

<name>

<part value="**FR-ANSM**"/>

</name>

</governingAuthority>

</territorialAuthority>

</primaryInformationRecipient>

<!-- ======================================================================-->

<!-- Just for illustration: here is an example of a document requested by an agency -->

<!-- For this example we use a specific document reference requested by French agency -->

<!-- Document Reference - Proof of Payment for France -->

<!-- =======================================================================-->

<derivedFrom>

<documentReference>

<id root="**1d7d9a00-e56b-4617-8d40-99aa81d84f98**"/>

</documentReference>

</derivedFrom>

</contextOfUse>

</component>

<!-- ========================================================================-->

<!-- Component Application Form -->

<!-- ========================================================================-->

<component>

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

<contextOfUse>

<!-- ========================================================================-->

<!-- Context of Use id root must be a unique identifier -->

<!-- ========================================================================-->

<id root="**ba7fb4f1-7305-4a67-8877-393e8d6fd343**"/>

<!-- ========================================================================-->

<!-- CTD Heading -->

<!-- ========================================================================-->

<code code="**100000164030**" codeSystem="2.16.840.1.113883.3.6905.7"/>

<!-- ========================================================================-->

<!-- Context of Use status code value is required and can only be "active" or "suspended" -->

<!-- ========================================================================-->

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

<!-- ========================================================================-->

<!-- Document reference for Application Form -->

<!-- ========================================================================-->

<derivedFrom>

<documentReference>

<id root="**f576787b-1bea-485f-82e8-26548e48ffbe**"/>

The document reference points to the document element where details of the referenced file are provided.

</documentReference>

</derivedFrom>

</contextOfUse>

</component>

....... <!-- *Additional information may appear* -->

<!-- ===================================================================-->

<!-- End of the submissionUnit element.-->

<!-- ===================================================================-->

</submissionUnit>

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

There are no additional requirements other than those outlined in the ICH eCTD IG.

## Document Reference

There are no additional requirements other than those outlined in the ICH eCTD IG.

## Submission Reference

The Submission Reference is designed to permit the sender to specify that a ***contextOfUse element*** does not apply to that submission (regulatory activity). The ***submissionReference*** element indicates the previously started regulatory activity to which the ***contextOfUse*** element must not be assigned.

In case a regulatory activity concerns several strengths of a medicinal product, but one of the strengths is not authorised, then the id element should point to the submission identifier to not present the content in the context of the indicated regulatory activity. For example: The change of a manufacturer for one of the excipients needs to be addressed, but for two of the five strengths covered by the dossier this excipient is not used. The change of the manufacturer is only relevant for three strengths and the manufacturer details can be hidden for those two forms not concerned.

### Location in XML

The ***submissionReference*** element follows the ***subjectOf*** element next to ***contextOfUse*** element:

* ***controlActProcess>> subject>> submissionUnit>>component>> contextOfUse>>subjectOf>>submissionReference***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***SubmissionReference*** element, and any special instructions.

*The* ***classCode*** *is fixed to “OBS” and* ***moodCode*** *is fixed to “EVN”. These values are not required in the XML message.*

***SubmissionReference.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Id*** |  | [1..1] |  | This is the container element of the following elements and attributes by which it uniquely  identifies the application. |
| ***Id.item*** |  | [1..\*] |  | This is a container element for  the ***SubmissionReference***. |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
|  | ***root*** | [1..1] | Valid OID or UUID | This is the root attribute that provides the global unique identifier for the  ***SubmissionReference*** element. |
| ***Conformance*** | The ***id.item@root*** is a required element  The ***id@extension*** is required when the ***id@root*** is 2.16.840.1.113883.3.989.2.2.1.13.1, and its value must be a valid Leaf Reference (i.e., it exists in the receiver’s system). | | | |
| ***Business Rules*** | More than one ***item*** element may be provided.  The submissionGroup element contains a negationIndication which will exclude a ***contextOfUse element*** from displaying for the indicated submission.  For forward compatibility, the document referenced from v3.2.2 will reuse its existing metadata for the document without changes. See ICH eCTD IG for further information. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id.item@identifierName*** * ***id.item@scope*** * ***id.item@reliability*** * ***id.item@displayable*** * ***id@validTimeLow*** * ***id@validTimeHigh*** * ***id@controlInformationRoot*** * ***id@controlInformationExtension*** * ***id@nullFlavor*** * ***id@flavorId*** * ***id@updateMode*** | | | |

***XMLSample: Submission Reference***

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

<subjectOf negationInd="**true**">

<submissionReference>

<id>

<item root="**76ac931c-9cc6-4cc8-bd94-0222e50a6adb**"/>

<item root="**34849ee7-a26b-4435-b269-43046a73e462**"/>

</id>

</submissionReference>

</subjectOf>

### Terminology

There is no further terminology foreseen.

## Keyword

The ***keyword*** element is used for the purpose of transmitting additional information about a ***contextOfUse*** element. In the EU M1, the Country Code will be used to specify commonly used or nationally used documents including the referenced files. The keywords to identify types of product information texts will be used for ***contextOfUse*** elements related to Module su.

The ***keyword*** is either defined by an external controlled vocabulary, e.g. Document Type Code, Language Code or Country Code, or it may be defined within the message as ***keywordDefinition***. For EU M1, the latter principle will apply to ***contextOfUse*** elements referencing product information texts in order to sort them according to pharmaceutical form or strength if relevant.

*Note: The life cycle will be executed by inserting a new contextOfUse element including the respective combination of keywords and by assigning the appropriate priority number. All life cycle considerations outlined in the ICH eCTD IG will apply to EU Module 1 in the same manner.*

### Location in XML

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

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

Refer to [[Table 4](bookmark://_bookmark45)](bookmark://_bookmark45): XML Structure for the XML representation.

### XML Details

There are no additional requirements other than those outlined in the ICH eCTD IG.

### Terminology

EU Module 1 controlled vocabularies are provided via [SPOR Web User Interface](https://spor.ema.europa.eu/sporwi/) (see section 6.1).

## Sequence Number

There are no additional requirements other than those outlined in the ICH eCTD IG. In case more than one sequence number needs to be provided (in case of grouped variations and work share procedures), the sequence number needs to be stated next to the application involved in the grouping or work shared procedure. Sequence numbers for grouping or work shared procedures need to follow agreed business rules (see section 10.3.1).

The title element can be completed as currently done for submission description.

## Submission

The ***submission*** is the representation of a regulatory activity constituted by several Submission Units and referring to exactly one application. The respective controlled vocabulary is EU specific.

A Submission Unit may contain more than one submission, each referring to one application (see section 5). This is relevant in the case of grouped variations or workshare procedures.

Remark: The id.item@root will change for a new regulatory activity only. As long as Submission Units refer to the same regulatory activity the same id@root will be used.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission***

Refer to Table 4: XML Structure for the XML representation.

### XML Details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***Submission*** element, and any special instructions.

*The* ***classCode*** *is fixed to “ACT” and* ***moodCode*** *is fixed to “EVN”. These values are not required in the XML message.*

***Submission.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***id*** |  | [1..1] |  | This is a container element that provides a unique identifier for  the submission. |
| ***id.item*** |  | [1..1] |  | This is the container element of the following attributes by which it uniquely identifies the application.  *Note: This is a regional constraint.* |
|  | ***root*** | [1..1] | Valid OID or UUID | This is the root attribute that  uniquely identifies the submission. |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
|  | ***extension*** | [1..n] | alpha-numeric e.g.  DE/H/1234/0 01-003/II/013 | The ***extension*** attribute of the ***id*** element provides a location to specify the EU procedure number including specific extensions related to the  regulatory activity. |
| ***Conformance*** | The ***id.item@root*** attribute is required for the ***submission*** element. | | | |
| ***Business Rules*** | Only one ***item*** element should be provided for a submission.  The ***id@extension*** is the extended procedure number for the regulatory activity. This value will stay the same for all Submission Units within  the regulatory activity. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id.item@identifierName*** * ***id.item@scope*** * ***id.item@reliability*** * ***id.item@displayable*** * ***id@validTimeLow*** * ***id@validTimeHigh*** * ***id@controlInformationRoot*** * ***id@controlInformationExtension*** * ***id@nullFlavor*** * ***id@flavorId*** * ***id@updateMode*** | | | |

***Submission.code***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***code*** |  | [0..1] |  | This is a container element for  the ***submission***. |
| ***code*** | [1..1] | Alpha Numeric  e.g., maa, var-  nat, var- type1b | This is the code attribute, which is a unique value that indicates the type of content in the ***submission***. |
| ***codeSystem*** | [1..1] | Valid OID or  GUID | This is the codeSystem attribute. |
| ***Conformance*** | There must be one, and only one, ***code@code*** attribute specified for a submission. | | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Business Rules*** | ***Submission*** codes may vary for different product types. In case of eCTD for  human medicinal product the relevant code list is referenced in section 6.1[.](#_bookmark35) | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***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*** | | | |

***Submission.statusCode***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***statusCode*** |  | [0..1] |  | This is a container element for the ***statusCode*** of the  submission. |
| ***code*** | [1..1] | Alpha Numeric  e.g., active, suspended | This is the ***statusCode*** attribute that indicates the status of the submission. |
| ***Conformance*** | If the ***statusCode*** element is provided, the ***code*** attribute is required. | | | |
| ***Business Rules*** |  | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***code@codeSystemName*** * ***code@codeSystemVersion*** | | | |

***XML sample: Submission***

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

<componentOf1>

<sequenceNumber value="**1**"/>

<submission>

<id>

<item root="**0d84467e-f20b-42ad-a69a-63e61a4f7ea7**" extension="**DE-H-1234-001-DC"**/>

</id >

<code code="**100000155689**” codeSystem="2.16.840.1.113883.3.6905.4/>

<!... displayName value="maa" as retrieved from the code system…!

</code>

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

<!..Additional information will follow in the **submission** element*.-->*

<componentOf>

<!..Additional information appears for the **application** element*. -->*

</componentOf>

</submission>

</componentOf1>

### Terminology

The ***submission*** element code values will be provided by EU-specific controlled vocabularies (see section 6.1).

The desired status codes will be used in line with ICH eCTD IG definitions.

### Related Elements

The ***following*** elements are related to ***submission*** and require additional information:

* ***subject2.review*** (see section 9.12)
* ***subject4.regulatoryReviewTime*** (not being used for EU)
* ***subject5.submissionGroup*** (see section 9.17)
* ***subject3.mode*** (see section 9.16)

## Contact Party

The ***callBackContact*** element is to be used for a person or department (***contactParty***) to contact if there are any questions. At least one Contact Party needs to be named per each Submission Unit. Therefore, it will always be the person authorised for communication on behalf of the applicant during the regulatory activity (running procedure) (code 2.4.2), regardless whether this is a member of staff of the applicant or of a third party acting on behalf of the applicant.

When submitting an initial eCTD v4.0 submission unit for an application, a technical contact party should be included for the purpose of troubleshooting any issues with the forward compatibility file. The following information should be sent for each technical contact.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>callBackContact>>contactParty***

Refer to Table 4: XML Structure for the XML representation.

### XML details

<!--Contact Parties are provided for the regulatory and technical contacts.-->

<callBackContact>

<contactParty>

<id root="**417e5c25-2001-40d1-af34-f1f285614187**"/>

<code code="**eu\_regulatory\_contact**" codeSystem="2.16.840.1.113883.3.6905.6"/>

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

<contactPerson>

<name>

<part type="**GIV**" value="**Anna**"/>

<part type="**FAM**" value="**Smith**"/>

</name>

<telecom xsi:type="**BAG\_TEL**">

<item value="**+331234-5678**" use="**WP**" capabilities="**voice**"/>

<item value="**+331234-5679**" use="**MC**" capabilities="**voice**"/>

<item value="**+331234-5670**" use="**WP**" capabilities="**fax**"/>

<item value="[**mailto:anna.smith@Wonderpharma.com**](mailto:anna.smith@Wonderpharma.com)"/>

</telecom>

<asAgent>

<representedOrganization>

<name>

<part value="**Wonderpharma Ltd.**"/>

</name>

</representedOrganization>

</asAgent>

</contactPerson>

</contactParty>

</callBackContact>

### Terminology

The ***ContactParty*** element requires codes for the code element (see section 6.1) and the statusCode element.

## Review

The ***review*** element provides a unique ID and is related to the regulatory activity (as defined by the submission) and is associated with the holder and an author in the meaning of the ReferenceMember State or responsible authority, e.g. EMA in Centralised procedures, and refers to the product and the product category. This ID may be used for a proper connection to a case management system.

For a new marketing authorisation application, details on the product category and the manufactured product are required from the applicant. For any other Submission Unit type and submission types these attributes should be ignored.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>subject2>>review***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

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

element, and any special instructions.

*The* ***classCode*** *is fixed to “REV” and* ***moodCode*** *is fixed to “RQO”. These values are not required in the XML message.*

***Review.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***id*** |  | [1..1] |  | This is a container element that  provides a unique identifier for the review activity. |
| ***root*** | [1..1] | Valid OID or UUID | This is the root attribute that uniquely identifies the review  activity. |
| ***Conformance*** | The ***id*** is a required element. | | | |
| ***Business Rules*** |  | | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id@extension*** * ***id@identifierName*** * ***id@scope*** * ***id@reliability*** * ***id@displayable*** | | | |

***XML Sample: Review***

The following is an example of the XML for the ***review*** element providing details on the product under review which will be only required in case of an initial MAA submission.

<subject2>

<!-- ===========================================================-->

<!-- Only one review element can exist for a message, which -->

<!-- is related to the regulatory activity and author in the meaning of RMS -->

<!-- ===========================================================-->

<review>

<id root="**bd6591d8-3aff-4330-8ffd-f6216634c784**"/>

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

<subject1>

<manufacturedProduct>

<id root="**3ee89f8c-7543-4b7f-868e-c1bd3042c024**"/>

<manufacturedProduct>

<!-- ===================================================-->

<!—This will work as the descrption of the pharmaceutical product and, therefore, >

<!— it should use the dosage form CV. This is a description independent from country. -->

<!-- ===================================================-->

<code code="**100000073665**" codeSystem="2.16.840.1.113883.3.6905.12">

<displayName value="**film-coated tablet**"/>

</code>

<!-- =======================================================-->

<!—If the name of the manufactured product is common in all countries involved or -->

<!—just one assingning territory relevant the product name should appear here. -->

<!-- =======================================================-->

One medicinal product name valid in all countries is exemplified as Case 2 in the following section.

<name>

<part value="**WonderPil**" language="**en**"/>

</name>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**France**"/>

</code>

<!-- =======================================================-->

<!—If the name of the manufactured product is specific in countries involved -->

<!—the product name should appear here followed by the assigning territory. -->

<!-- =======================================================-->

</assigningTerritory>

</asNamedEntity>

==============================-->

….

<!-- =======================

<!-- ACTI = active ingredient -->

Different medicinal product names valid in the involved countries are exemplified as Case 1 in the following section.

<!-- =====================================================-->

<ingredient classCode="**ACTI**">

<ingredientSubstance>

<name>

<!-- ===================================================-->

<!-- 100000090270 TermID for PARACETAMOL in EUTCT -->

<!-- ===================================================-->

<part code="**100000090270**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**PARACETAMOL**"/>

</name>

</ingredientSubstance>

</ingredient>

</manufacturedProduct>

</manufacturedProduct>

</subject1>

<holder>

<applicant>

<sponsorOrganization>

<name>

<!-- ======================================================-->

<!—Company name of the Marketing Authorisation Applicant, identified by LOC-ID of OMS -->

<!-- ======================================================-->

<part codeSystem="2.16.840.1.113883.3.6905.y.y" code="**ORG-100002779**" value="**Bayer Sante**"/>

<part codeSystem="2.16.840.1.113883.3.6905.x.x" code="**LOC-100010224**" value="**Loos, France**"/>

</name>

</sponsorOrganization>

</applicant>

</holder>

<author>

<territorialAuthority>

<!-- ======================================================-->

<!—Territory the governing authority responsible for -->

<!-- ======================================================-->

<territory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displaName value="**FR**"/>

</code>

</territory>

<governingAuthority>

<name>

<!-- ======================================================-->

<!-- Assessment authoring authority -->

<!-- ======================================================-->

<part code="**100000160631**" codeSystem="2.16.840.1.113883.3.6905.10" value="**FR-ANSM**"/>

</name>

</governingAuthority>

</territorialAuthority>

</author>

<subject2>

<!-- ======================================================-->

<!-- Only one Product Category element can exist for a message -->

<!-- Product Category: Medicinal product containing chemical substance -->

<!-- 100000155527 = "Chemical" in RMS -->

<!-- ======================================================-->

<productCategory>

<code code="**100000155527**" codeSystem="2.16.840.1.113883.3.6905.13"/>

</productCategory>

</subject2>

<subject3>

<regulatoryStatus>

<!-- ======================================================-->

<!-- The regulatory status element is excluded for applicant submission units. -->

<!-- It will only be used by regulators once two-way-communication will be implemented -->

<!-- in future. In that case, the example is provided as -->

<!-- TermID 100000072097 = Application for Marketing Authorisation received -->

<!-- ======================================================-->

<code code="**100000072097**" codeSystem="2.16.840.1.113883.3.6905.5"/>

</regulatoryStatus>

</subject3>

</review>

</subject2>

### Related Elements

The ***following*** elements are related to ***review*** and require additional information:

* ***subject1.manufacturedProduct*** (see section 9.13)
* ***holder.applicant*** (see section 9.19)
* ***subject2.productCategory*** (see section 9.15)

## Manufactured Product

This element must be selected in the case of an eCTD v4.0 message concerning the initial Marketing Authorisation Application for a human medicinal product. This determines the assessment of a product in the national context within a DCP or MRP or may trigger internal procedural decisions. Subsequent Submission Units related to authorised products do not need to provide this type of information repeatedly.

The ***manufacturedProduct*** element collects the name of the product by country and the active ingredients. This element may support internal workflow mechanisms but will not yet replace the annex 5.19 to the application form of the current Module 1.2 in the EU.

Once a common product data base is accessible, the ID may be taken from that data base. This option needs to be detailed in a future version of this Implementation Guide.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>subject2>>review>>subject1>>manufacturedProduct***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***manufacturedProduct*** element in case it is provided, and any special instructions.

*The* ***classCode*** *is fixed to “MANU”. This value is not required in the XML message.*

***ManufacturedProduct.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Id*** |  | [1..1] |  | This is a container element for a reference to the manufactured  product. |
| ***root*** | [1..1] | Valid OID or UUID | This attribute is for a global unique identifier of the ***manufactured product*** being  referenced. |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Conformance*** | The ***id*** element and ***root*** attribute are required. | | | |
| ***Business Rules*** | This element provides the referencing point for the invented name of the medicinal product per involved member state. In case of **initial** MAA, these elements may provide the respective name of the manufactured product as proposed for the country the authorisation is applied for. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id@extension*** * ***id@identifierName*** * ***id@scope*** * ***id@reliability*** * ***id@displayable*** | | | |

***XML Sample: manufacturedProduct***

See example of the XML for the ***review*** element.

### Related Elements

The following element is related to ***manufacturedProduct*** and requires additional information:

* ***manufacturedProduct.name*** (This element needs to be extended to assign the country where the product name is proposed to be used)
* ***manufacturedProduct.ingredient*** (This element is restricted to class code ACTI, which means the active ingredient only**)**

***Product with attributes on ingredients and territory the product name is valid for***

The ***manufacturedProduct*** element provides information about the name of the product in each applicable territory, and its ingredient(s), depending on how many pharmaceutical active ingredients are contained. There are options to mention the different product names per assigned territory for that same manufactured product (case 1) or to include the one product name and list of active ingredients valid in all involved member states (case 2):

Case 1

To cover the different product names (e.g., WonderPil, WonderDrug, WunderMittel), in this sample the ***product.name.item.part*** is repeated and connected with the ***assignedTerritory*** element as many as member states are involved. The repeated ***assignedTerritory*** element is indicated by . See alson example of the XML for the ***review*** element (Section 9.12).

<subject2>

<review>

<id root="**9fcd4db3-8337-4814-8216-24b89759e307**"/>

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

<subject1>

<manufacturedProduct>

<id root="**3ee89f8c-7543-4b7f-868e-c1bd3042c024**"/>

<manufacturedProduct>

<code code="**100000073665**" codeSystem="2.16.840.1.113883.3.6905.12">

<displayName value="**film-coated tablet**"/>

</code>

<asNamedEntity>

<name> <part value="**WonderPil**" language="**fr**"/> </name>

<assigningTerritory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**France**"/>

</code>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<name>

<part value="**WonderDrug**" language="**fr**"/>

</name>

<assigningTerritory>

<code code="**100000000337**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**Belgium**"/>

</code>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<name>

<part value="**WunderMittel**" language="**de**"/>

</name>

<assigningTerritory>

<code code="**100000000403**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**Germany**"/>

</code>

</assigningTerritory>

</asNamedEntity>

<ingredient classCode="**ACTI**">

<ingredientSubstance>

<name>

<part code="**100000090270**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**PARACETAMOL**"/>

</name>

</ingredientSubstance>

</ingredient>

</manufacturedProduct>

</manufacturedProduct>

</subject1>

<author>

<territorialAuthority>

<name><part code="**100000160631**" codeSystem="2.16.840.1.113883.3.6905.10" value="**FR-ANSM**"/></name>

</territorialAuthority>

</author>

<subject2>

<productCategory>

<code code="**100000155527**" codeSystem="2.16.840.1.113883.3.6905.13"/>

</productCategory>

</subject2>

</review>

</subject2>

Case 2

In this sample the product name WonderPil is identical in all member states. Therefore, the assigning territory is repeated without repeating the name part (as indicated by ):

<subject2>

<review>

<id root="**9fcd4db3-8337-4814-8216-24b89759e307**"/>

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

<subject1>

<manufacturedProduct>

<id root="**156c1fc5-9c27-49e5-942d-1d96b0052e59**"/>

<manufacturedProduct>

<code code="**100000073665**" codeSystem="2.16.840.1.113883.3.6905.12">

<displayName value="**film-coated tablet**"/>

</code>

<name> <part value="**WonderPil**" language="**fr**"/> </name>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**France**"/>

</code>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000337**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value=" **Belgium** "/>

</code>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000403**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value=" **Germany** "/>

</code>

</assigningTerritory>

</asNamedEntity>

<ingredient classCode="**ACTI**">

<ingredientSubstance>

<name>

<part code="**100000090270**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**PARACETAMOL**"/>

</name>

</ingredientSubstance>

</ingredient>

<ingredient classCode="**ACTI**">

<ingredientSubstance>

<name>

<part code="**100000013146**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**CAFFEINE**"/>

</name>

</ingredientSubstance>

</ingredient>

</manufacturedProduct>

</manufacturedProduct>

</subject1>

<author>

<territorialAuthority>

<name>

<part code="**100000160631**" codeSystem="2.16.840.1.113883.3.6905.10" value="**FR-ANSM**"/>

</name>

</territorialAuthority>

</author>

<subject2>

<productCategory>

<code code="**100000155527**" codeSystem="2.16.840.1.113883.3.6905.13"/>

</productCategory>

</subject2>

</review>

</subject2>

## Holder

This element is referencing the details of the ***applicant*** element (see Section 9.19) and will be executed only there.

## Product Category

The ***productCategory*** is used to indicate the overall category of human medicinal product based on the active ingredients, e.g. chemical, herbal or biotech product.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>subject2>>review>>subject2>>productCategory***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***productCategory*** element, and any special instructions.

*The* ***classCode*** *is fixed to “CATEGORY” and* ***moodCode*** *is fixed to “EVN”. These values are not required in the XML message.*

***productCategory.code***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Code*** |  | [1..1] |  | This is a container element for  the ***productCategory***. |
|  | ***code*** | [1..1] | Alpha Numeric  e.g., “Chemical”, “Herbal” | This is the ***code*** attribute for the coded value of the ***productCategory***. |
|  | ***codeSystem*** | [1..1] | Valid OID or UUID | This is the ***codeSystem*** attribute that is a unique identifier for the controlled vocabulary system. |
|  |  |  |  | *This should be the OID or UUID registered for the code system.* |
| ***Conformanc e*** | The ***code*** and ***codeSystem*** are required elements. | | | |
| ***Business Rules*** |  | | | |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***code@codeSystemName*** * ***code@codeSystemVersion*** * ***code@valueSet*** * ***code@valueSetVersion*** * ***code@controlInformationExtension*** * ***code@controlInformationRoot*** * ***code@flavourId*** * ***code@id*** * ***code@nullFlavour*** * ***code@updateMode*** * ***code@validTimeHigh*** * ***code@validTimeLow*** * ***code@xsi:type*** * ***code@codingRationale*** * ***code@translationcode@source*** | | | |

***XML Sample: productCategory***

See example of the XML for the ***review*** element.

### Terminology

The ***productCategory*** element requires codes for the ***code*** element (see section 6.1).

## Mode

The high-level handling of the information submitted as part of variation(s) and extension applications will be indicated by this element. The ***mode*** element should only be used in variation or extension regulatory activities and must be included in every sequence of that activity. The following are the valid modes: a single regulatory activity (e.g. a Type II variation), a grouped activity (e.g. several variations grouped into a single submission, a periodic report of type IA variations applicable to one or more marketing authorisations), and an activity subject to a worksharing agreement (e.g. a Type II variation applicable to more than one marketing authorisation or a PSUR single assessment procedure).

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>subject3>>mode***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

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

element, and any special instructions.

*The* ***classCode*** *is fixed to “POLICY” and* ***moodCode*** *is fixed to “EVN”. These values are not required in the XML message.*

***mode.code***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Element** | **Attribute** | | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Code*** |  | | [1..1] |  | This is the ***code*** attribute for the coded value of the mode of a  submission. |
| ***code*** | | [1..1] | Alpha Numeric  e.g. “single” | This is the ***code*** attribute for the coded value of the mode of the submission type variation. |
| ***codeSystem*** | | [1..1] | Valid OID or UUID | This is the ***codeSystem*** attribute that is a unique identifier for the controlled vocabulary system.  *This should be the OID or UUID registered for the code system.* |
| ***Conformance*** | The ***code*** and ***codeSystem*** are required attributes. | | | | |
| ***Business Rules*** | The mode element should only be used in variation or line extension regulatory  activities and must be included in every sequence of that activity. | | | | |
| **Element** | **Attribute** | **Cardinality** | | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***code.realmCode*** * ***code.typeId*** * ***code.templateId*** * ***code@codeSystemName*** * ***code@codeSystemVersion*** * ***code@controlInformationExtension*** * ***code@controlInformationRoot*** * ***code@flavourId*** * ***code@id*** * ***code@nullFlavour*** * ***code@updateMode*** * ***code@validTimeHigh*** * ***code@validTimeLow*** * ***code@valueSet*** * ***code@valueSetVersion*** * ***code@codingRationale*** * ***code@xsi:type*** | | | | |

***XML Sample: mode***

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

<componentOf1>

<sequenceNumber value="**2**"/>

<submission>

<id>

<item root="**76ac931c-9cc6-4cc8-bd94-0222e50a6adb**"/>

</id>

<!-- ====================================================-->

<!-- Application Submission Type code -->

<!-- Initial Marketing Authorisation Application Term-ID = 100000155689 -->

<!-- ====================================================-->

<code code="**100000155689**" codeSystem="2.16.840.1.113883.3.6905.4"/>

<subject3>

<mode>

<!-- ====================================================-->

<!--The mode element should only be used in variation or line extension-->

<!-- regulatory activities and must be included in every sequence of that activity -->

<!-- 100000155556 = Regulatory activity subject to a worksharing agreement -->

<!-- ====================================================-->

<code code="**100000155556**" codeSystem="2.16.840.1.113883.3.6905.16" value="**worksharing**"/>

</mode>

</subject3>

<!-- ====================================================-->

<!--Additional information may appear. -->

<!-- ====================================================-->

</submission>

</componentOf1>

See [XML Colour Legend](#_bookmark2) for colour usage

### Terminology

The ***mode*** element requires codes for the code element (see section 6.1).

## Submission Group

The Submission Group represents an option to process regulatory activities together in case the assessment will cover the same content and applies to more than one product which will otherwise not be assessed together, e.g. several generic applications with different product names, but identical pharmaceutical composition and properties. A submission group needs to be defined per regulatory activity and is required to be stated within each Submission Unit submitted during that course of assessment.

The ***submissionGroup*** element can be used where the same regulatory activity will be processed the same way, but formerly not running under a grouping or worksharing procedure number. The UUID will connect the different applications for processing the submission (regulatory activity) as a group.

See section 10.3.1 for further reference.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componenOf1>> submission>>subject5>>submissionGroup***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***submissionGroup*** element, and any special instructions.

*The* ***classCode*** *is fixed to “GROUPER” and* ***moodCode*** *is fixed to “EVN”. These values are not required in the XML message.*

***submissionGroup.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Id*** |  | [1..1] |  | This is a container element that provides a unique identifier for the submission group that the submission is part of. |
|  | ***root*** | [1..1] | Valid UUID | The ***root*** attribute of the ***item*** element provides a global unique identifier for the submission  reference. |
| ***Conformance*** | The ***id@root*** is a required attribute. | | | |
| ***Business Rules*** | The same ID needs to be added to all group members. This will indicate a group of applications the regulatory activity applies to. They are not formally defined as a grouping or worksharing, but in case of duplicates they can be processed together. The sender of the message may decide whether the activities will be processed in this way or not. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id@identifierName*** * ***id@extension*** * ***id@scope*** * ***id@reliability*** * ***id@displayable*** * ***id@validTimeLow*** * ***id@validTimeHigh*** * ***id@controlInformationRoot*** * ***id@controlInformationExtension*** * ***id@nullFlavor*** * ***id@flavorId*** * ***id@identifierName*** * ***id@updateMode*** * ***id@xsi:type*** | | | |

***XML Sample: submissionGroup***

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

<subject5>

<submissionGroup>

<id root="**UUID for the submissionReference**"/>

</submissionGroup>

</subject5>

### Terminology

There is no further terminology foreseen.

## Application

The a***pplication*** element represents a request from Regulated Industry to a Regulatory Authority, for the approval to market a medicinal product for human use. The application, in this context, will typically cover all dosage forms and strengths of a product. In the Centralised Procedure, this will be equivalent to all dosage forms and strengths covered by an EMA application number (e.g. EMEA/H/C/000123). In MRP/DCP, a single eCTD application should, preferably, be used for the procedure (e.g. DE/H/2087/001-sss/DC or MR). However, if an applicant decides not to apply for all strengths and dosage forms in every member state in the procedure, the possibility of having one eCTD application per strength/dosage form should be considered.

Referencing across applications is possible when all content is identifiable by using an eCTD v4.0 compliant identifier. Content previously submitted according to the eCTD v3.2.2 specification can be referenced using the appropriate mechanism as detailed in ICH eCTD IG Section 8.1.1 and Section 9.2.17.1.

An application will consist over time of multiple submissions or regulatory activities (e.g. initial marketing authorisation application, variations or PSURs) over time. For example, a marketing application may consist of one or more regulatory decisions e.g., the collection of all approvals is related to the application. Each regulatory submission (for details refer to [section](#_bookmark35) 6.1 for controlled vocabulary of Application Submission Types) will have its own regulatory action, and most likely will be composed of one or more Submission Units.

Several types of application can be differentiated as outlined in Annex 1 of the Directive 2001/83/EU and reflected in the ***code*** element (see below section 9.18.3 Terminology).

The ***application*** element is also presented in the ICH eCTD IG, as it is the connection point for the ***document*** and ***keywordDefinition*** elements in the XML message, but only complementary information is provided.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application***

Refer to Table 4: XML Structure for the XML representation.

### XML details

There are no additional requirements other than those outlined in the ICH eCTD IG.

<componentOf>

<application>

<id>

<!-- ==========================================-->

<!-- Root reflects the UUID introduced in eCTD v3.2.2-->

<!-- Extension reflects the European procedure number in this example -->

<!-- Code reflects the legal basis of the application, e.g. -->

<!-- New active substance (Article 8(3) of Directive No 2001/83/EC)-->

<!-- ==========================================-->

<item root="**5f0e8436-e1df-4031-90d3-413deff109e5**" extension="**FR/H/0001/001/DC**"/>

</id>

<code code="**100000116047**" codeSystem="2.16.840.1.113883.3.6905.2"/>

**…**

</application>

### Terminology

The controlled terminology for the ***application*** element includes codes for application types (e.g. Full Dossier, Bibliographic, Biosimilar, Generic) (refer to section 6.1).

### Related Elements

The ***following*** elements are related to ***application*** and require additional information:

* ***holder.applicant*** (see section 9.19)
* ***informationRecipient.territorialAuthority*** (see section 9.20)
* ***subject.reviewProcedure*** (see section 9.21)
* ***reference.applicationReference*** (see section 9.22)
* ***component.document.*** (see section 9.23)
* ***referencedBy.keywordDefinition*** (see section 9.24)

## Applicant

The ***applicant*** element is used to provide the sponsor details of a marketing authorisation application***.***

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application>>holder>>applicant***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***applicant*** element, and any special instructions.

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

***SponsorOrganization.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Id.item*** |  | [1..1] |  | This is the container element of the following elements and attributes by which it uniquely  identifies the applicant. |
| ***root*** | [1..1] | Valid OID | The ***root*** attribute of the ***id.item***  element provides the OID for OMS |
| ***extension*** | [1..1] | LOC-100020264 | The ***extension*** attribute of the ***id*** element provides a location to specify the LocID from  OMS. |
| ***Conformance*** | The ***id.item@root*** attribute is required for the ***applicant*** element. | | | |
| ***Business Rules*** | The ***id*** element should only have one ***item*** element.  The ***id.item@extension*** should be the LocID from OMS that is on record for the company name provided in the ***name*** element. | | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id.item@identifierName*** * ***id.item@scope*** * ***id.item@reliability*** * ***id.item@displayable*** * ***id@validTimeLow*** * ***id@validTimeHigh*** * ***id@controlInformationRoot*** * ***id@controlInformationExtension*** * ***id@nullFlavor*** * ***id@flavorId*** * ***id@updateMode*** | | | |

***SponsorOrganization.name***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***name.part*** |  | [1..1] |  | This is the container element that organises the value of  applicant’s name. |
| ***value*** | [1..1] | String  e.g. Wonder Pharma AG | This attribute is for the value of the name part of the Applicant. |
| ***Conformance*** | The ***name.part@value*** attribute is required. | | | |
| ***Business Rules*** | The applicant’s name should represent the OID of the OMS that is on record for  the company name that is provided in the identifier value. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***name.part@code*** * ***name.part@codeSystem*** * ***name.part@codeSystemVersion*** * ***name.part@language*** * ***name.part@nullFlavor*** * ***name.part@qualifier*** * ***name.part@xsi:type*** | | | |

### Excluded Elements

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

* ***applicant.sponsorOrganization.addr***
* ***Applicant.sponsorOrganization.telecom***

To provide contact information, see Section 9.11 for contact party instructions.

***XML Sample: applicant***

Example:

<holder>

<applicant>

<sponsorOrganization>

<id>

<item root=”OMS OID” extension=”**LOC-100020264**”/>

</id>

<name>

<part value="**Bayer Sante**"/>

</name>

</sponsorOrganization>

</applicant>

</holder>

## Territorial Authority (as information recipient related to application)

This element refers to the applicable recipients receiving the Submission Unit / Submission and being involved in the procedure. The recipients need to be named for each country where the

medicinal product is applied to be marketed.

The ***territorialAuthority*** element indicates the country for which the authority decision will be relevant and which NCA is the recipient in cases where more than one is responsible to authorise medicinal products in one country, e.g. PEI for vaccines and BfArM for herbal medicinal products in Germany.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application>>informationRecipient>>territorialAuthority >>governingAuthority***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

For the complete set of XML elements and attributes required for the ***territorialAuthority*** element see section 9.4 [.](#_bookmark56)

*The* ***classCode*** *is fixed to “TERR”. This value is not required in the XML message.*

***XML Sample reflecting subelements of componentOf***

The following is an example of the XML for the subelements ***application, applicant, informationRecipient, reviewProcedure and applicationReference***.

<componentOf>

<application>

<id>

<!-- ================================================-->

<!-- Root reflects the UUID introduced in eCTD v3.2.2. -->

<!-- Extension reflects the EU procedure number, in this example FR/H/0001/001/DC -->

<!-- ================================================-->

<item root="**5f0e8436-e1df-4031-90d3-413deff109e5**" extension="**FR/H/0001/001/DC**"/>

</id>

<code code="**100000116047**" codeSystem="2.16.840.1.113883.3.6905.2">

<displayName value="**Article 8(3) of Directive Nr. 2001/83/EC**"/>

</code>

<holder>

<applicant>

<sponsorOrganization>

<id>

<item root="**9gpon8436-l23w-4zb1-20g3-8d3deff1ta01**"/>

</id>

<name xsi:type="**EN**">

<part code="**ORG-123456789**" codeSystem="2.16.840.1.113883.3.6905.y.y" value="**WPhLtd.**"/>

<part code="**LOC-987654321**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**Paris, France**"/>

</name>

<!-- ================================================-->

<!-- The id.root may reflect the OID (LOC-ID) of the OMS and name part for -->

<!-- the company name. Address details of the company location can be retrieved -->

<!-- from OMS as well. Code LOC-654321 is the identifier provided by SPOR OMS-->

<!-- (codeSystem="2.16.840.1.113883.3.6905.x.x") for the applicant company. -->

<!-- Any additional address details or phone numbers will be ignored if provided. -->

<!-- ================================================-->

</sponsorOrganization>

</applicant>

</holder>

<informationRecipient>

<territorialAuthority>

<!-- =====================================================-->

<!—The territory can be named, but is an optional element. If it is used the code -->

<!—and codeSystem must be provided. The displayName will retrieved from the system.-->

<!-- =====================================================-->

<territory>

<item code="**100000000403**" codeSystem="2.16.840.1.113883.3.6905.18"/>

<displayNamevalue="**Germany**"/>

<territory>

<governingAuthority>

<name>

<part code="**100000160623**" codeSystem="2.16.840.1.113883.3.6905.10" value="**DE-PEI**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160750**" codeSystem="2.16.840.1.113883.3.6905.2.10" value="**NL-MEB**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<subject>

<reviewProcedure>

<code code="**100000155060**" codeSystem="2.16.840.1.113883.3.6905.9" value="**Decentralised Procedure**"/>

</reviewProcedure>

</subject>

<reference>

<!-- ================================================-->

<!--Reference to an originator product-->

<!-- ================================================-->

<applicationReference>

<id root="**5b887340-6510-4648-8c49-b561c5967c16**" extension="**ema002156-001**"/>

<reasonCode>

<!-- ================================================-->

<!-- Reference medicinal product chosen for the demonstration of bioequivalence -->

<!-- ================================================-->

<item code="**100000155053**" codeSystem="2.16.840.1.113883.3.6905.3" value="**BE-Ref-Product**"/>

</reasonCode>

</applicationReference>

</reference>

</application>

</componentOf>

The following is an example of the XML for the ***territorialAuthority*** element in case multiple concerned member states have to be included.

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160631**" codeSystem="2.16.840.1.113883.3.6905.10" value="**FR-ANSM**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160750**" codeSystem="2.16.840.1.113883.3.6905.10" value=" **NL-MEB**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160772**" codeSystem="2.16.840.1.113883.3.6905.10" value=" **DE-BFARM**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160762**" codeSystem="2.16.840.1.113883.3.6905.10" value="**AT-AGES**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

### Terminology

The name of the territory is provided in the respective controlled vocabulary (see section 6.1).

## Review Procedure

The ***reviewProcedure*** element defines the type of procedure to assess the marketing authorisation application whether it is a Centralised, Decentralised, Mutual Recognition or purely National procedure.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application>> subject>>reviewProcedure***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***reviewProcedure*** element, and any special instructions.

*The* ***classCode*** *is fixed to “POLICY” and* ***moodCode*** *is fixed to “EVN”. These values are not required in the XML message.*

***reviewProcedure.code***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Code*** |  | [1..1] |  | This is a container element that provides a unique identifier for  the review procedure type code. |
| ***code*** | [1..1] | Valid OID or UUID | This is the code attribute that  uniquely identifies the review procedure type. |
|  | ***codeSyste m*** | [1..1] | Valid OID or UUID | This is the ***codeSystem*** attribute that is a unique identifier for the controlled vocabulary system.  *This should be the OID or UUID registered for the code system.* |
| ***Conformance*** | The ***code*** is a required element. | | | |
| ***Business Rules*** | The review procedure type needs to be provided in each case. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***code@codeSystemName*** * ***code@codeSystemVersion*** * ***code@codingRationale*** * ***code@controlInformationExtension*** * ***code@controlInformationRoot*** * ***code@flavorId*** * ***code@id*** * ***code@nullFlavor*** * ***code@updateMode*** * ***code@validTimeHigh*** * ***code@validTimeLow*** * ***code@valueSet*** * ***code@valueSetVersion*** * ***code@xsi:type*** | | | |

***XML Sample: reviewProcedure***

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

<subject>…

<reviewProcedure>

<!-- ================================================-->

<!-- The review procedure defines the type of procedure to assess the MAA -->

<!-- e.g. Decentralised Procedure which relates to TermID = 100000155060 in RMS -->

<!-- ================================================-->

<code code="**100000155060**" codeSystem="2.16.840.1.113883.3.6905.9" value="**Decentralised Procedure**"/>

</code>

</reviewProcedure>

…

</subject>

### Terminology

The ***reviewProcedure*** element requires codes for the ***code*** element (see section 6.1).

## Application Reference

The ***applicationReference*** element provides the type of reference for generic products. Therefore, the element is required only where a reference need to be provided. The product confirming the data protection period has expired and the reference product being used in the bioequivalence study have to be stated. In all cases the authorisation number should be provided.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application>>reference>>applicationReference***

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

The following tables provide a complete set of XML elements and attributes required for the

***applicationReference*** element, and any special instructions.

*The* ***classCode*** *is fixed to ACT and moodCode is fixed to EVN. The values are not required in the XML message.*

***ApplicationReference.id***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Id*** |  | [1..1] |  | This is a container element of the following attributes by which it uniquely identifies the application  being referenced. |
| ***root*** | [1..1] | Valid OID or UUID | This attribute is for a global unique identifier. |
| ***extension*** | [1..1] | Alpha Numeric  *e.g.*  *FR/H/1234/ 001/MR* | The ***extension*** attribute of the ***id*** element provides a location to specify the authorisation number being referenced. |
| ***Conformance*** | The ***id*** is a required element, if the ***applicationReference*** element is provided. | | | |
| ***Business Rules*** | This element must be used three times in the case of generic products indicating the expiry of the data protection period, the reference made regarding a  nationally marketed product and the reference used in the bioequivalence study. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***id@identifierName*** * ***id@scope*** * ***id@reliability*** * ***id@displayable*** * ***id@validTimeLow*** * ***id@validTimeHigh*** * ***id@controlInformationRoot*** * ***id@controlInformationExtension*** * ***id@nullFlavor*** * ***id@flavorIdid@updateMode*** * ***id@xsi:type*** | | | |

***ApplicationReference.reasonCode***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Item*** |  | [1..1] |  | This is the container element for  the reason for the reference. |
| ***code*** | [1..1] | Alpha  Numeric | This is the code attribute that  uniquely identifies the reason. |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
|  | ***codeSystem*** | [1..1] | Valid OID or UUID | The codeSystem is a unique identifier that indicates the controlled vocabulary system.  *This should be the OID or UUID registered for the code system.* |
| ***Conformance*** | The ***code*** is a required element. | | | |
| ***Business Rules*** | This element is required if a reference is provided. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***item@codeSystemName*** * ***item@codeSystemVersion*** * ***item@valueSet*** * ***item@valueSetVersion*** * ***item@codingRationale*** * ***item@controlInformationExtension*** * ***item@controlInformatioRoot*** * ***item@flavorId*** * ***item@id*** * ***item@nullFlavor*** * ***item@updateMode*** * ***item@validTimeHigh*** * ***item@validTimeLow*** * ***item@xsi:type*** | | | |

***XML Sample: application reference***

The following is an example of the XML for the application reference information.

<reference>

<!-- ================================================-->

<!--Reference to an originator product-->

<!-- ================================================-->

<applicationReference>

<id root="**5b887340-6510-4648-8c49-b561c5967c16**" extension="**ema002156-001**"/>

<reasonCode>

<!-- ================================================-->

<!-- Reference medicinal product chosen for the demonstration of bioequivalence -->

<!-- The code for “**BE-Ref-Product**” = “100000155053” -->

<!-- ================================================-->

<item code="**100000155053**" codeSystem="2.16.840.1.113883.3.6905.3" value="**BE-Ref-Product**"/>

</reasonCode>

</applicationReference>

</reference>

### Terminology

The ***applicationReference.reasonCode*** element requires codes for the ***item*** element, e.g. expiry of data protection period (see section 6.1).

## Document

The ***document*** element is used for the purposes of transmitting the information about each document related to an application. The valid use for a specific application and the purpose of a specific regulatory activity is based on the association with a specified CoU. As documents will not be deleted or set to inactive (no status change is foreseen), a new CoU can be associated at any time regardless of whether the application itself is still active or the regulatory activity is rejected or approved.

***Document*** elements (referencing e.g. PDF files) will be prepared by the sender, i.e. the Applicant, for review by the Regulatory Authority, or the Regulatory Authority for sending a Submission Unit to Applicants. A ***document*** element is applicable to one file and is referenced by one ***contextOfUse*** element. The same CoU element combinations may be used in multiple Submission Units (re-use of documents)1[4](#_bookmark138). Document Re-use using Forward Compatibility is detailed in ICH eCTD IG Section 9.2.17.1. Documents can be grouped using a group title provided with the ***contextOfUse*** element. To the ***contextOfUse*** element an additional label can be assigned if the document title is not instructive enough or too general or too detailed.

Coding of documents regarding confidentiality may be applied. For the time being this element remains optional as different business rules may apply in different member states. Therefore, no final version of a controlled vocabulary can be offered. However, the confidentiality code is only able to indicate, that the content needs to be checked.

### Location in XML

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

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application>>component>>document***

14 The CTD granularity document specifies where one or more documents may be submitted for each CTD section. Because the eCTD v3.2.2 does not distinguish between files and documents, those terms have been previously used interchangeably. The granularity document has been updated to specify the opportunities when using eCTD v4.0. (<http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R4_Organisation/M4_R4> Granularity\_Doc ument.pdf)

Refer to Table 4: XML Structure for the XML representation.

### XML details

***XML Elements***

Tables with a complete set of XML elements and attributes required for the ***document*** element are provided in the ICH eCTD IG and will not be repeated here. The following additional requirements apply for EU M1.

***document.text***

|  |  |
| --- | --- |
| ***Business Rules*** | In the EU: The ***text*** element should be used when sending a document.  The ***text@language*** should be provided for document elements referenced by the EU M1 CoU codes m1-3-1.  The ***text@mediaType*** should be provided if there is a special file format.  The ***text.thumbnail*** element will not be used by the receiving party.  The ***value*** attribute is for the sender’s use only, and ***text.thumbnail*** is provided at the discretion of the sender.  The ***text.description@value*** attribute is not thought to be used in the context of EU M1.  For file reuse, the d***ocumentReference*** element provides the UUID of the  ***document*** element to be re-used. It is prerequisíte that the metadata as well as the content cannot be changed for any re-use. |
| ***Excluded***  ***Elements and Attributes*** | No other elements than indicated in the ICH eCTD v4.0 IG will be excluded. |

***Document.confidentialityCode***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***confidentialityCode*** |  | [0..1] |  | This is a container element that provides an ability to identify Commercial Confidential Information (CCI) and Protected  Personal Data (PPD) in the EU. |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed *Examples*** | **Description**  ***Instructions*** |
|  | ***code*** | [1..1] | Valid OID or UUID  (e.g. Confidential, Public, Restricted) | This is the ***code*** attribute that contains the value for the  confidentiality code. |
|  | ***codeSystem*** | [1..1] | Valid OID or UUID | This is the ***codeSystem*** attribute that is a unique identifier for the controlled vocabulary system.  *This should be the OID or UUID registered for the code system.* |
| ***Conformance*** | The ***confidentialityCode*** is an optional element. | | | |
| ***Business Rules*** | If the element is provided, a code and a codeSystem attribute are required. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***confidentialityCode.displayName*** * ***confidentialityCode.originalText*** * ***confidentialityCode.translation*** * ***confidentialityCode.source*** * ***confidentialityCode@codeSystemName*** * ***confidentialityCode@codeSystemVersion*** * ***confidentialityCode@valueSet*** * ***confidentialityCode@valueSetVersion*** * ***confidentialityCode@codingRationale*** * ***confidentialityCode@validTimeLow*** * ***confidentialityCode@validTimeHigh*** * ***confidentialityCode@controlInformationRoot*** * ***confidentialityCode@controlInformationExtension*** * ***confidentialityCode@nullFlavor*** * ***confidentialityCode@flavorId*** * ***confidentialityCode@id*** * ***confidentialityCode@updateMode*** * ***confidentialityCode@xsi:type*** | | | |

***XML Samples***

The following are examples of the XML for ***document*** elements. The Document is a component of an Application.

Sample 1:

<component>

<document>

<id root="**50cf78aa-7c32-4994-859b-49500369fe1d**"/>

<title value="**General Information**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**" charset=" **utf8**">

<reference value="**../m1/nongmo-var.pdf**"/>

<!-- ================================================-->

<!-- Thumbnail is an optional attribute which may be used by the sender for internal -->

<!—purposes (e.g. DMS ID), but will be ignored by the receiver. -->

<!-- ================================================-->

<thumbnail value="**identifier for document from sender's document management system**"/>

<integrityCheck>**56df6492f724ee2e76e12cb4b001bd2fdc43603 fb15d70afc89813398739fb9c**</integrityCheck>

<!-- ================================================-->

<!-- Description is an optional attribute which is thought not to be used for EU M1. -->

<!-- ================================================-->

<description>**Normally not provided**</description>

</text>

</document>

</component>

Sample 2:

<component>

<document>

<id root="**16d152de-3258-4523-a21b-0abe5b01fe82e**"/>

<title value="**Cover Letter for DE**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**de**">

<reference value="**../m1/de-cover.pdf**"/>

<integrityCheck>**b9a6aff775736cf100505af68da859a941432a9f9e56d24 5ac3edaa4235df0ac**</integrityCheck>

</text>

<!-- ================================================-->

<!-- Commercial Confidential Information and Protected Personal Data-PPD in EU: -->

<!-- L =Low -->

<!-- M=Moderate -->

<!-- N=Normal -->

<!-- U=Unrestricted -->

<!-- R=Restricted -->

<!-- V=Very Restricted -->

Or

<!-- Confidential -->

<!-- Public -->

<!-- Restricted -->

<!-- ================================================-->

<confidentialityCode code="**Restricted**" codeSystem=" 2.16.840.1.113883.3.6905.2.x.xx.x"/>

</document>

</component>

|  |
| --- |
| *Note to Implementers: For documents (i.e. each representing a single file), the text element will be provided along with the other required elements.* |

### Terminology

The ***document*** element has one coded terminology for language (the ISO language codes) (see section 6.3).

### Document Reuse

Document reuse is the ability to submit a document once to a Regulatory Authority and refer to the document by its unique identifier in future submissions if the document is validly retained by the Regulatory Authority.

Document reuse will only be possible if the files has been previously submitted (just submitted and not approved) and are validly retained. Hence this functionality cannot be used widely in all NCAs (and EU procedures) until the [Common Repository](https://esubmission.ema.europa.eu/central_repository.HTML) is set up for his purpose. However, can be used form the beginning for all EMA CAPs.

Documents can be referenced/reused without resubmitting the physical file by referencing each document unique identifier. This can occur:

- Across a submission unit.

- Across regulatory activities within an application.

- Across different applications.

All the contents of the reused document, including references and hypertext links to other documents, should be relevant to the submission that reuses the document.

The ***documentReference*** element provides the UUID of the document element to be re-used.

Examples of document reuse can be seen in section 10.3.2.

## Keyword Definition

The ***keywordDefinition*** element is used by the sender to define a keyword that is referenced by an identifier in other parts of the message. For details see the ICH Implementation guide. The usage of this element is expected to be helpful in EU Module 1 for product information text to separate different strengths in addition to the keywords as mentioned earlier (see section 9.8).

The purpose is to support presentation of content that shall be displayed together and will provide a meaningful orientation for reviewers.

### Location in XML

The document element in the XML message is in the following location:

* ***controlActProcess>> subject>> submissionUnit>>componentOf1>> submission>>componentOf>>application>>referencedBy>>keywordDefinition***

Refer to Table 4: XML Structure for the XML representation.

### XML details

Tables with a complete set of XML elements and attributes required for the ***keywordDefinition*** element are provided in the ICH eCTD IG and will be specified for EU M1 purpose here. The following requirements apply for EU M1.

##### ***keywordDefinition.code***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***Code*** |  | [1..1] |  | This is a container element that provides an ability to identify sender defined keywords. |
| ***code*** | [1..1] | Text  e.g eu\_keyword\_definition\_type\_2 | The code attribute for the coded value of the type of keyword definition. |
|  | ***codeSystem*** | [1..1] | Valid OID    Numeric, i.e. 2.16.840.1.113883.3.989.5.1.2.2.1.100 | The codeSystem attribute provides a unique identifier that indicates the controlled vocabulary system.  This should be the OID registered for the code system |
| ***Conformance*** | The code and codeSystem are required attributes. | | | |
| ***Business Rules*** | The code must be from a valid EU Keyword code type. | | | |
| ***Excluded Elements and Attributes*** | The following attributes are not required by eCTD 4.0:   * ***code.displayName*** * ***code.originalText*** * ***code.translation*** * ***code.source*** * ***code@codeSystemName*** * ***code@codeSystemVersion*** * ***code@codingRationale*** * ***code@controlInformationRoot***   ***code@controlInformationExtension***   * ***code@nullFlavor*** * ***code@flavorId*** * ***code@id*** * ***code@validTimeLow*** * ***code@validTimeHigh*** * ***code@updateMode*** * ***code@valueSet*** * ***code@valueSetVersion*** * ***code@xsi:type*** | | | |
| ***Excluded Elements and Attributes*** | No other elements than indicated in the ICH eCTD v4.0 IG will be excluded. | | | |

##### *keywordDefinition.statusCode*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Element** | | | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** | |
| ***statusCode*** | |  | | [1..1] |  | | This is the container element that identifies the status of the ***keywordDefinition.*** |
|  | | ***code*** | | [1..1] | Alpha  *e.g., active* | | The ***code*** attribute provides the value for the status. |
| ***Conformance*** | The statusCode is required.. | | | | | | |
| ***Business Rules*** | The code attribute should always have a value of "active". | | | | | | |
| ***Excluded Elements and/or Attributes*** | The following datatype elements and attributes may not be required by eCTD v4.0:  • statusCode@controlInformationExtension  • statusCode@controlInformationRoot  • statusCode@flavorId  • statusCode@nullFlavor  • statusCode@updateMode  • statusCode@validTimeHigh  • statusCode@validTimeLow  • statusCode@xsi:type | | | | | | |
|  |  |  |  |  |  |  |  |

##### *keywordDefinition.value*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Element** | **Attribute** | **Cardinality** | **Value(s) Allowed**  ***Examples*** | **Description**  ***Instructions*** |
| ***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. |
| ***code*** | [1..1] | Alpha  e.g. FIGURE\_UNIT | The ***code*** attribute provides for the keyword being defined. |
| ***codeSystem*** | [1..1] | Text  Sender-defined value | The ***codeSystem*** value that is a unique identifier for the controlled vocabulary system. |
| ***value.item.displayName*** |  | [1..1] |  | This is the container element specify the ***displayNam***e, which is the value of the ***keywordDefinition*** code***.*** |
| ***value*** | [1..1] | Text  Sender-defined value | The ***displayName*** attribute of the value element of the keyword being defined. |
| ***updateMode*** | [0..1] | Alpha  e.g. R for Replace | The ***updateMode*** should be used to make changes to the Keyword Definition’s display name value. |
| ***Conformance*** | The ***keywordDefinition.value*** is a required element.  The ***value.item@code***, ***value.item@codeSystem*** and ***value.item.displayName@value*** are required attributes.  If there is a conflict with the ***keywordDefinition.value.item@code*** and ***keywordDefinition.value.displayName*** – i.e., an update is not being made with ***updateMode*** and a new ***displayName@value*** is provided for an existing code, the submission unit will be rejected. | | | |
| ***Business Rules*** | See ICH IG | | | |
| ***Excluded Elements and/or Attributes*** | See ICH IG | | | |

### Guidance regarding Keyword Definition values

For EU M1 currently one sender defined keyword type is in use: eu\_keyword\_definition\_type\_2. It is describing the strength of the manufactured pharmaceutical form. It consists of a value and the related unit of measurement as provided in the respective controlled vocabulary at SPOR-RMS: https://spor.ema.europa.eu/rmswi/#/lists/100000110633/terms. The code “FIGURE\_UNIT” reflects this concatenation. The OID of the keywordDefinition code system is defined as 2.16.840.1.113883.3.989.5.1.2.2.1.100.

**XML Samples**

The following is an example of the XML for keywordDefinition element at application level and its use for a contextOfUse element at submissionUnit level.

PORP\_IN000001UV ITSVersion="**XML\_1.0**" xmlns="**urn:hl7-org:v3**" xmlns:xsi="**http://www.w3.org/2001/XMLSchema-instance**" xsi:schemaLocation="**urn:hl7-org:v3 PORP\_IN000001UV.xsd**">

<id/>

<controlActProcess classCode="**ACTN**" moodCode="**EVN**">

<subject typeCode="**SUBJ**">

Submission Unit

<submissionUnit>

<id root="**c503dce7-d628-42c1-861a-ab738afe739d**"/>

<code code="**100000155047**" codeSystem="2.16.840.1.113883.3.6905.1"/>

<title value="**Initial**"/>

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

<component>

<priorityNumber value="**1800**"/>

Context of Use

<contextOfUse>

<id root="**d55b4f72-4fe7-462b-9720-dcb3b8ed988c**"/>

<code code="**100000164032**" codeSystem="2.16.840.1.113883.3.6905.7">

<originalText value="**m1/131-smpc.pdf**"/>

</code>

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

<derivedFrom>

Document

<documentReference>

<id root="**af90684b-8650-4b8f-aa49-dda2da086e6c**"/>

</documentReference>

</derivedFrom>

<referencedBy typeCode="REFR">

<keyword>

Keywords for documents properties in its context of use

<code code="**100000155538**" codeSystem="2.16.840.1.113883.3.6905.14.1"/>

</keyword>

Keyword on product information document type

</referencedBy>

<referencedBy typeCode="**REFR**">

<keyword>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.10.1"/>

</keyword>

Keyword on country

</referencedBy>

<referencedBy typeCode="**REFR**">

<keyword>

<code code="**100000072175**" codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.101.1"/>

</keyword>

Keyword on language

</referencedBy>

<referencedBy typeCode="**REFR**">

<keyword>

<code code="**FIGURE\_UNIT**" codeSystem="**CustomCodes1**"/>

</keyword>

Sender defined keyword on strength

</referencedBy>

<referencedBy typeCode="**REFR**">

<keyword>

<code code="**100000073665**" codeSystem="2.16.840.1.113883.3.6905.12.1"/>

</keyword>

Keyword on manufactured pharmaceutical form

</referencedBy>

</contextOfUse>

</component>

More details inbetween

<componentOf1>

<sequenceNumber value="**1**"/>

<submission>

More details inbetween

<subject2>

More details inbetween

<review/>

</subject2>

<componentOf>

<application>

<id>

<!-- ================================================-->

<!-- Root reflects the UUID introduced in eCTD v3.2.2. -->

<!-- Extension reflects the EU procedure number, in this example FR/H/9001/001/DC -->

<!-- ================================================-->

<item root="**5f0e8436-e1df-4031-90d3-413deff109e5**" extension="**fr9001**"/>

</id>

More details inbetween

<component>

<document>

Referenced documents

<id root="**af90684b-8650-4b8f-aa49-dda2da086e6c**"/>

<title value="**Summary of Product characteristics**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**">

<reference value="**m1/131-smpc.pdf**"/> <integrityCheck>**aa3857911141cde703c4473241b7548a88b37ee1376a4dd9a224a9e0c0b5ff81**</integrityCheck>

</text>

<confidentialityCode code="**L**" codeSystem="2.16.840.1.113883.3.6905.x.x"/> </document>

</component>

<referencedBy>

Sender defined keyword definition

<keywordDefinition> <code code="**eu\_keyword\_definition\_type\_2**" codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.100.1"/>

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

<value>

<item code="**FIGURE\_UNIT**" codeSystem="**CustomCodes1**">

<displayName value="**150\_mg**" validTimeLow="**NA**"/>

</item>

</value>

</keywordDefinition>

</referencedBy>

</application>

</componentOf>

</submission>

</componentOf1>

</submissionUnit>

</subject>

</controlActProcess>

</PORP\_IN000

|  |  |
| --- | --- |
| A black and white chat bubble with a wrench and a white symbol  Description automatically generated | *Note to Implementers: It is not foreseen to re-submit keywordDefinition values in each sequence. However, sender defined keywords can be modified but will executed then for all applications making use of them.* |

# CREATING THE MESSAGE

With the individual components of the XML message described above, each of those components will now be used to demonstrate how to compose multiple components to address a specific scenario. This will also explain how to address the creation and modifications to the content transmitted during the lifecycle of a submission focusing on EU Module 1, as recommendations need to differ from ICH recommendations to cover EU specific scenarios. Therefore, this section will provide samples dealing with elements not used commonly in ICH, e.g. manufacturedProduct, submissionMode, territorialAuthority, as well as regulatory activities used specifically in the EU such as grouped variation, workshare procedures and submissions in Decentralised and Mutual Recognition Procedures.

## Individual Components

### Managing Country-Specific Product Names in MRP and DCP

Different from the Centralised and purely national procedures, in MRP and DCP different product names per Member State may occur. Not copying content from the annexes of the application form, but supporting agency specific processing, the product names related to the territory of the assigning authority can be stated in ***ManufacturedProduct***, and related elements.

***XML example for different product names (case 1) or one product name (case 2) in different member states in MRP/DCP:***

Case 1

<subject1>

<manufacturedProduct>

<id root="**156c1fc5-9c27-49e5-942d-1d96b0052e59**"/>

<manufacturedProduct>

<!-- =======================================================-->

<!-- To have multiple product names (e.g. WunderMittel in Germany, WonderDrug in Belgium, -->

<!-- WonderPil in France) the elements name and asNamedEntity are repeated as necessary. -->

<!-- =======================================================-->

<name/>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**France**"/>

</code>

<name>

<part value="**WonderPil**" language="**fr**"/>

</name>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000337**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**Belgium**"/>

</code>

<name> <part value="**WonderDrug**" language="**fr**"/> </name>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000403**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**Germany**"/>

</code>

<name>

<part value="**WonderMittel**" language="**de**"/>

</name>

</assigningTerritory>

</asNamedEntity>

<ingredient classCode="**ACTI**">

<ingredientSubstance>

<name>

<part code="**100000090270**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**PARACETAMOL**"/>

</name>

</ingredientSubstance>

</ingredient>

</manufacturedProduct>

</manufacturedProduct>

</subject1>

Case 2

<subject1>

<manufacturedProduct>

<id root="**156c1fc5-9c27-49e5-942d-1d96b0052e59**"/>

<manufacturedProduct>

<!-- =======================================================-->

<!-- To have one product name valid in different countries the element asNamed Entity will -->

<!-- be repeated as necessary. At all time, one assiningTerritory is required. The attribute will -->

<!-- language may be omitted in that case. -->

<!-- =======================================================-->

<name>

<part value="**WonderPil**"/>

</name>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**France**"/>

</code>

</assigningTerritory>

<asNamedEntity>

</asNamedEntity>

<assigningTerritory>

<code code="**100000000337**" codeSystem="2.16.840.1.113883.3.6905.18"/>

<displayName value="**Belgium**"/>

</code>

</assigningTerritory>

</asNamedEntity>

<asNamedEntity>

<assigningTerritory>

<code code="**100000000403**" codeSystem="2.16.840.1.113883.3.6905.18"/>

<displayName value="**Germany**"/>

</code>

</assigningTerritory>

</asNamedEntity>

<ingredient classCode="**ACTI**">

<ingredientSubstance>

<name>

<part code="**100000090270**" codeSystem="2.16.840.1.113883.3.6905.x.x" value="**PARACETAMOL**"/>

</name>

</ingredientSubstance>

</ingredient>

</manufacturedProduct>

</manufacturedProduct>

</subject1>

### Managing Country Specific Processing Numbers

Only in the case of MRP and DCP, multiple national procedure numbers need to be stated in addition to the procedure number. The latter is inserted as UUID of the application. The ***application.id.item*** element will be repeated as many times as needed. The extension provides the container for a national procedure number.

***XML example:***

<componentOf>

<application>

<id>

<item root="5f0e8436-e1df-4031-90d3-413deff109e5" extension="de-2189072"/>

<item root="5f0e8436-e1df-4031-90d3-413deff109e5" extension="nl-456789"/>

<item root="5f0e8436-e1df-4031-90d3-413deff109e5" extension="mt-341974”/>

<item root="5f0e8436-e1df-4031-90d3-413deff109e5" extension="fr-234-345"/>

</id>

<!-- =======================================================-->

<!-- Additional information may appear after the addition of the Application.code, -->

<!-- for example any of the following elements related to Application – component, -->

<!-- referencedBy, informationRecipient,reference, subject, or holder] -->

<!-- =======================================================-->

</application>

</componentOf>

### Product Information Texts in EU Module 1.3.1

Product information texts need to have a set of metadata to specify the country of applicability, the language, the type of text and, depending on the product structure, information regarding pharmaceutical form or strength. These metadata will be assigned using different elements of the eCTD XML message:

* + - * The ***document.text*** element holds a ***language*** element. The codes are provided from the controlled vocabulary of ISO language codes (see section 6.3).
      * The ***contextOfUse*** element holds a ***keyword*** element specifying PI document types like “smpc” or “pl”, and a ***keyword*** element specifying the country the product information document is applicable to.
      * The country codes are provided from the controlled vocabulary of ISO country codes (see section 6.3). The controlled vocabulary of document types is provided by SPOR RMS (see section 6.1).
      * A keyword value from the sponsor defined ***keywordDefinition*** of pharmaceutical form or strength will allow presentation on the set of product information texts provided in the QRD template for pharmaceutical form or strength.
      * The ***text.thumbnail*** element will not be used by the receiving party. The ***value*** attribute is for the sender’s use only, and ***text.thumbnail*** is provided at the discretion of the sender.
      * The ***text.description@value*** attribute may be used by the applicant for internal purposes. This description will be ignored in the EU for document elements in this section m1.3.

The keyword value for pharmaceutical form must not use a standard term according to EDQM. The purpose of this value is just to differentiate the product presentations and should be as simple as possible.

***XML example:***

Context of Use element referencing a document element

<component>

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

<contextOfUse>

<id root="**872f0cb1-472a-4440-aac1-46605bdd8d7f**"/>

<!-- ================================================-->

<!-- CTD Heading -->

<!-- ================================================-->

<code code="**100000164031**" codeSystem="2.16.840.1.113883.3.6905.7">

<originalText value="**1.3.1 SmPC, Label, PL**"/>

</code>

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

<setId root="**set ID**"/>

<versionNumber value="**1.0**"/>

<primaryInformationRecipient>

<!-- ================================================-->

<!-- Specific Health Authority and/or country to which this CoU is for (primaryInformation-->

<!-- Recipient element restricts the display of the document exclusively to that Authority) -->

<!-- ================================================-->

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160750**" codeSystem="2.16.840.1.113883.3.6905.2.10" value="**NL-MEB**"/>

</name>

</governingAuthority>

</territorialAuthority>

</primaryInformationRecipient>

<derivedFrom>

<documentReference>

<id root="**af90684b-8650-4b8f-aa49-dda2da086e6c**" extension="**12345**"/>

</documentReference>

</derivedFrom>

<subjectOf negationInd=”**true**”/>

<!-- ================================================-->

<!-- The **submissionReference** element is used to indicate when a **contextOfUse** is -->

<!-- not relevant to a specific submission within a **submissionUnit**.-->

<!-- ================================================-->

<submissionReference>

<id>

<item root="**96cff057-c634-4b68-aa8e-bedd8a0dade3**" extension="**DE-H-1234-001-DC** "/>

</id>

</submissionReference>

<referencedBy typeCode="**REFR**">

<keyword>

<!-- ================================================-->

<!-- The Context Of Use will provide the document type keyword and country the -->

<!-- product information text document applies to*.*.-->

<!-- ================================================-->

<code code="**100000155532**" codeSystem="2.16.840.1.113883.3.6905.7" value="**SmPC**"/>

</keyword>

</referencedBy>

<referencedBy typeCode="**REFR**">

<keyword>

<!-- ================================================-->

<!--Providing not a code system requires the existence of a keyword definition -->

<!-- provide for this application (see end of the message or any previous -->

<!-- submissionunit.xml within the life cycle.-->

<!-- ================================================-->

<code code="**FORM01**"/>

</keyword>

</referencedBy>

</contextOfUse>

</component>

Numerous lines will normally appear to indicate submission details, and reference to the application provided. The following indicates the document element:

<componentOf>

<application>

<component>

<document>

<id root="**af90684b-8650-4b8f-aa49-dda2da086e6c**"/>

<title value="**Summary of Product characteristics**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**"/>

<reference value="**../m1/131-smpc.pdf**"/>

<integrityCheck>**3285a776897425b9a3b87abbaaf163fb2646726ec91242397 997b003efe3203e**</integrityCheck>

<text/>

<confidentialityCode code="**L**" codeSystem="2.16.840.1.113883.3.6905.x.x"/>

</document>

</component>

</application>

</componentOf>

Proposed code:

<component>

<priorityNumber value="**2000**"/>

<contextOfUse>

<id root="**cd7fzuf1-1783-4d2w-8op7-4163e8dtxo19**"/>

<!-- ================================================-->

<!-- CTD Heading -->

<!-- ================================================-->

<code code="**100000164032**" codeSystem="2.16.840.1.113883.3.6905.7">

<originalText value="**m1/131-pl.pdf**"/>

</code>

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

<!-- ================================================-->

<!—Additional information will follow to reference the document and their keywords-->

<!-- Recipient element restricts the display of the document exclusively to that Authority) -->

<!-- ================================================-->

</component>

<componentOf1>

<sequenceNumber value="**1**"/>

<submission>

<id/>

<code/>

<callBackContact>

<!-- =========================================================-->

<!— relevant details will be added -->

<!-- =========================================================-->

</callBackContact>

<subject2/>

<subject3/>

<subject5/>

<componentOf>

<application>

<id>

<!-- =========================================================-->

<!-- Root reflects the UUID introduced in eCTD v3.2.2. -->

<!-- Extension reflects the EU procedure number, in this example FR/H/9001/001/DC --

<!-- ========================================================= -->

<item root="**5f0e8436-e1df-4031-90d3-413deff109e5**" extension="**fr9001**"/>

</id>

<code code="**100000116047**" codeSystem="2.16.840.1.113883.3.6905.2">

<displayName value="**New active substance (Article 8(3) of Directive No 2001/83/EC)**"/>

</code>

<holder/>

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160750**" codeSystem="2.16.840.1.113883.3.6905.2.10" value="**NL-MEB**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<subject/><subject/>

<reference/>

<component>

<document>

<id root="**f576787b-1bea-485f-82e8-26548e48ffbe**"/>

<title value="**Package Leaflet**"/><title value="**Package Leaflet**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**">

<reference value="**m1/131-pl.pdf**"/>

<integrityCheck>**89e3515ca2ad03190ed1897a9ce3a2d2219a0ae512be17339e047b1  
721166a43**</integrityCheck>

</text>

<confidentialityCode code="**L**" codeSystem="2.16.840.1.113883.3.6905.x.x"/>

</document>

</component>

<referencedBy>

<!-- ================================================-->

<!-- The Context Of Use will provide the document type or product information document type keyword, -->

<!-- country and manufactured pharmaceutical form the product information text document applies to.. -->

<!-- For strength a sender defined KeywordDefinition need to be provided here.-->

<!-- ================================================-->

<keywordDefinition>

<code code="**eu\_keyword\_definition\_type\_2**" odeSystem="**2.16.840.1.113883.3.989.5.1.2.2.1.100.1**" />

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

<value>

<item code="**FIGURE\_UNIT**" codeSystem="**CustomCodes1**">

<displayName value="**150\_mg**" validTimeLow="**NA**" />

</item>

</value>

</keywordDefinition>

</referencedBy>

<referencedBy>

<keywordDefinition>

<code code="**eu\_keyword\_definition\_type\_2**" codeSystem="**2.16.840.1.113883.3. 989.5.1.2.2.1.100.1**"

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

<value>

<item code="**FIGURE\_UNIT**" codeSystem="**CustomCodes1**">

<displayName value="**160\_mg**" updateMode="**R**" />

</item>

</value>

</keywordDefinition>

</referencedBy>

<!-- ================================================-->

<!-- Using a sender defined keyword requires a defining code system, which need to be established -->

<!-- in advanced (see end of the message or any previous submissionunit.xml within the life cycle. -->

<!-- ================================================-->

<referencedBy>

<keywordDefinition>

<code code="**RIM\_System\_List**" codeSystem="**Bayer\_KeywDef\_01**"/>

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

<value>

<item code="**Master54**" codeSystem="**RIM\_System\_List**">

<displayName value="**Standard**" validTimeLow="**NA**"/>

</item>

</value>

</keywordDefinition>

</referencedBy>

</application>

## Content Life Cycle Management (contextOfUse and Documents)

There are no deviating principles to apply when an eCTD v4.0 XML message is sent to a European Competent Authority, in comparison to the general rules set out by ICH. The example below shows a short sample of ***contextOfUse*** and ***Document*** elements referencing a few EU Module 1 files.

***XML example:***

<componentOf>

<application>

<!-- ================================================-->

<!-- Additional information may appear after the **Application.code**, for example any-->

<!-- of the following elements related to **holder, informationRecipient,** -->

<!-- **ReviewProcedure, Application.Reference**-->

<!-- ================================================-->

<component>

<document>

<id root="**88c5b0a4-8042-4110-a0c2-af8e51d87e26**"/>

<title value="**Cover Letter**"/>

<text integrityCheckAlgorithm="**SHA256"** language**="en"** charset**="utf-8">**

**<**reference value**="../m1/common-cover-20120420.pdf"**/>

<integrityCheck>**3285a776897425b9a3b87abbaaf163fb261242397997b003efe3201e**</integrityCheck>

</text>

<confidentialityCode code="**L**" codeSystem="2.16.840.1.113883.3.6905.x.x"/>

</document>

</component>

<component>

<document>

<id root="**b4db2ef3-cb0a-4fd7-be1c-2875e0ae7193**"/>

<title value="**Tracking Table**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**" charset="**utf-8**">

<reference value="**../m1/common-cover-tracking-20120420.pdf**"/>

<integrityCheck>**3285a776xv745a25b9a3b87abbaaf163f726ec912423979 97b003efe3201e**</integrityCheck>

<description value= = "**Does not seem to be necessary**"/>

</text>

</document>

</component>

<component>

<document>

<id root="**3bd2276d-fa45-47c7-9360-fa833cffbb1f**"/>

<title value="**Expert Quality**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**" charset="**utf-8**">

<reference value="**../m1/quality-meier.pdf**"/>

<integrityCheck>**3285a776897425b9a3b877z45abbaaf1726ec912423979 97b003efe3202e**</integrityCheck>

</text>

<confidentialityCode code="**L**" codeSystem="2.16.840.1.113883.3.6905.x.x"/>

</document>

</component>

<component>

<document>

<id root="**0b4229b0-6c98-4fe9-9575-556019c12fc5**"/>

<title value="**Expert Non-Clinical**"/>

<text integrityCheckAlgorithm="**SHA256**" language="**en**" charset="**utf-8**">

<reference value="**../m1/nonclinical-schulz.pdf**"/>

<integrityCheck>**3285a776897425b9a3b87abbaaf163fb2646726ec912423979 97b003efe3203e**</integrityCheck>

</text>

</document>

</component>

</application>

</componentOf>

The respective folder structure is provided in Figure 3, below:

A white rectangular object with a black border

Description automatically generated

**Figure 3: Folder structure related to Submission Unit message**

## Complex Scenarios

### Grouped Submissions

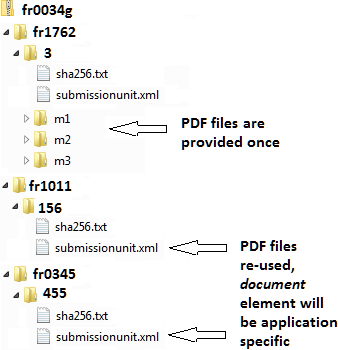
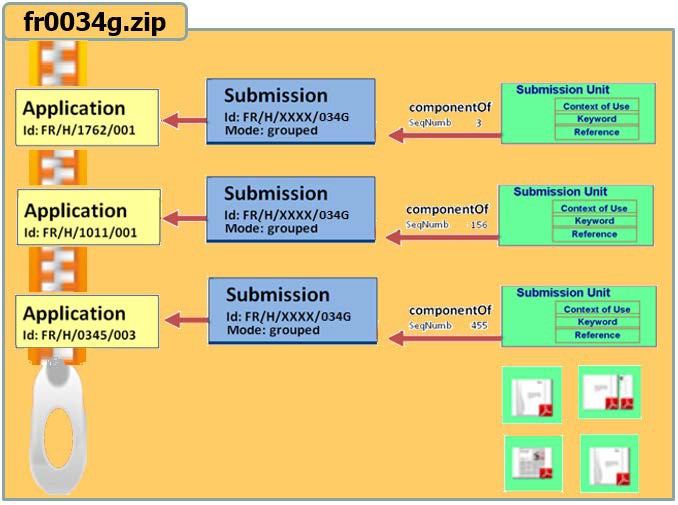
A grouped submission is defined as a regulatory activity that impacts multiple dossiers, based on regulatory requirements.

In EU, grouped submission functionality of eCTD 4.0 consists of sending multiple submission units included in one transmission (providing one submissionunit.xml for each application involved and referencing the PDF files submitted together with one of the submissionunit.xml files). See Figure 4 below.

Grouped submissions takes advantage of document reuse functionality, allowing the applicant to include only once, in one submission unit, all the concerned physical files. The submissionunit.xml will contain ***contextOfUse*** elements only for one application and references the document element UUIDs included from e.g., fr1762 submissionunit.xml by which the files are provided. However, each Submissionunit.xml file contains the identical grouping or WS procedure number to serve as the connecting element.

The use of grouped submissions functionality is optional to the applicant and does not prevent to submit each submission unit with each own content at any time.

In terms of Forward compatibility conversion, if an application is included in an eCTD v4.0 grouped submission, all applications are considered to have switched to eCTD v4.0 whereas a v3.2.2 grouped submission cannot reference v4.0 applications.

**Figure 4: Referencing multiple applications using multiple XML files**



### Examples of Document Reuse and/or Grouped Submissions

1. **Worksharing Variation:** The use of document reuse would be useful when providing identical content for the different NP/MRP/DCP applications concerned. or when applying for CEP/ASMF changes, DS Analytical Methods, PhV Systems, etc.

1. **Grouping Variation:** The use of document reuse would be useful when providing identical content for the different MAAs involved.

1. **ASMF (Active Substance Master Files):** The introduction of Applicant’s Part of Module 3 documents can be referenced using document reuse functionality across applications.

1. **PSUR (Periodic Safety Update Reports):** The introduction of PSUR report under Module 5 (section 5.3.6 Reports of Post-Marketing Experience) can be referenced using document reuse functionality across applications.

1. **Duplicate Applications in MRP/DCP procedures:** As a duplicate is an independent authorised medicinal product, there is no definition of a “duplicate” in the pharmaceutical legislation. However, for practical purpose, a duplicate application is defined by reference to the first application or marketing authorisation as follows:

- same dossier (copy of modules 1, 2, 3, 4 and 5).

- same legal basis according to Directive 2001/83/EC, as amended.

- different tradename.

- same or different applicant/marketing authorisation holder.

1. **Re-submission of regulatory activities (i.e., variations, etc.):** When a given variation needs to be re-submitted, some of the documents already provided are identical. By document reusing, there would be no need to introduce again on the submission unit.

1. **Any document that can be used across applications:**
   1. Common documents on Module 1 (1.4 Experts, Application form annexes, 1.8 Pharmacovigilance, Common responses for duplicated dossiers, etc.)
   2. Common literature references placed on Module 3 (3.3), Module 4 (4.3) or module 5 (5.4).
   3. Any other common document placed under any dossier section.

### Update of Product Information Texts (SmPC, PL) in Response to Regulators Assessment of a Grouped Variation

Based on a PRAC recommendation an update of the wording of the SmPC and PL for a number of products across a range of MAs is required to be submitted as a Type II variation in grouping mode. France is the RMS with Malta, Ireland and the Netherlands as CMS. The previously submitted documents will be replaced.

Set of documents provided:

|  |  |  |  |
| --- | --- | --- | --- |
| **Grouped ID Mode: Grouped** | **Virtual variation number (not included in the XML but would be included in the cover letter)** | **Sequence number per application** | **Documents separated by product name and member state** |
| id: FR/H/xxxx/II/003G | FR/H/1762/001/II/002/G | 19 | Pile Wonder 10mg tablets - FR Wonder Pills 10mg tablets - MT &IR Wonder Drug 10mg tablets - NL |
| id: FR/H/xxxx/II/003G | FR/H/1762/002/II/002/G | 19 | Pile Wonder 20mg tablets -FR Wonder Pills 20mg tablets - MT &IR Wonder Drug 20mg tablets - NL |
| id: FR/H/xxxx/II/003G | FR/H/1011/001/II/003/G | 54 | Pile Wonder 10mg capsules - FR Wonder Pill 10mg capsules - MT& IR Wonder Drug 10mg capsules - NL |
| id: FR/H/xxxx/II/003G | FR/H/0345/001/II/003/G | 24 | Pile Wonder 10mg/ml Solution for Infusion - FR Wonder Pill 10mg/ml Solution for Infusion - MT & IR  Wonder Drug 10mg/ml Solution for Infusion - NL |

***XML sample:***

<?xml version="**1.0**" encoding="**UTF-8**"?>

<!== ================ Reference Instance for EU ======================>

<PORP\_IN000001UV ITSVersion="**XML\_1.0**" xmlns="**urn:hl7-org:v3**" xmlns:xsi="<http://www.w3.org/2001/XMLSchema-instance>" xsi:schemaLocation="**urn:hl7-org:v3 PORP\_IN000001UV.xsd**">

<id/>

<creationTime/>

<interactionId/>

<processingCode/>

<processingModeCode/>

<acceptAckCode/>

<receiver>

<device classCode="**DEV**" determinerCode="**INSTANCE**">

<id>

<item root="**2.16.840.1.113883.3.989.2.2.1.11.1**" identifierName="**ICH eCTD v4.0 IG v1.3**"/>

<item root="**2.16.840.1.113883.3.989.5.1.1.6.1.1**" identifierName="**EU M1 IG v1.0**"/>

</id>

</device>

</receiver>

<sender>

<device classCode="**DEV**" determinerCode="**INSTANCE**">

<id/>

</device>

</sender>

<controlActProcess classCode="**ACTN**" moodCode="**EVN**">

<subject typeCode="**SUBJ**">

<submissionUnit>

<id root="**c503dce7-d628-42c1-861a-ab738afe739d**"/>

<code code="**100000164059**" codeSystem="2.16.840.1.113883.3.6905.1">

<title value="**Response to Question**"/>

</code>

<statusCode code="active"/>

<component>

This section needs to be repeated as often as CoU needs to be included, e. g. for cover letter, tracking table, variation form and PL

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

<contextOfUse>

<id root="**872f0cb1-472a-4440-aac1-46605bdd8d7f**"/>

<code code="**m131-smpclabelpl**" codeSystem="2.16.840.1.113883.3.6905.6">

<originalText value="**1.3.1 SmPC, Label ,PL**"**/**>

</code>

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

<primaryInformationRecipient>

<territorialAuthority>

<territory>

<code code="**100000000395**" codeSystem="2.16.840.1.113883.3.6905.18">

<displayName value="**France**"/>

</code>

</territory>

<governingAuthority>

<name>

<part code="**100000160631**" codeSystem="2.16.840.1.113883.3.6905.10" part value="**FR- ANSM**"/>

</name>

</governingAuthority>

</territorialAuthority>

|  |  |  |
| --- | --- | --- |
|  | | This section will point to the previous version of the SmPC and will be repeated as frequently as documents will  be replaced. |
| **59842345687**"/> |  |
|  |
|  | |

</primaryInformationRecipient>

<replacementOf typeCode ="**RPLC**">

<relatedContextOfUse>

<id root="**87454521-9874-6541-1236-1**

</relatedContextOfUse>

</replacementOf>

<subjectOf negationInd="**true**">

<submissionReference>

<id>

<item root="**76ac931c-9cc6-4cc8-bd94-0222e50a6ad**"/>

</id>

</submissionReference>

</subjectOf>

<referencedBy typeCode="**REFR**">

<keyword>

<code code="**100000000395** codeSystem="2.16.840.1.113883.3.6905.10" "/>

</keyword>

</referencedBy>

</contextOfUse>

</component>

<componentOf1 >

<sequenceNumber value="**19**"/>

<submission>

<id>

<item root="**0c083bd9-4ee7-40a9-8c33-5ab22f084d8e**" extension="**FR/H/XXXX/IA/034/G**"/>

</id>

<code code="**100000155693**" codeSystem="2.16.840.1.113883.3.6905.4">

<displayName value="**maa**"/>

</code>

This section needs to be repeated as often as member states are involved in the procedure

The sequence number and following attributes including information recipient and application attribute need to be created in case of grouped submissions separately for each dossier to support a simple collection of all submission unit files per dossier once needed.

<callBackContact>

In case of grouped submissions the legal base is quite not Article 8(3) as shown here. The legal base could be a variation or a pharmacovigilance single assessment procedure instead.

<contactParty> …

</contactParty>

</callBackContact>

<subject2>

<review>

</review>

</subject2>

<subject3>

<mode>

<code code="**grouped**"/>

</mode>

</subject3>

<componentOf>

<application>

<id>

<item root="**fr-1762-001-dc**" extension="**fr-2189072**"/>

</id>

<code code="**100000116047**" codeSystem="2.16.840.1.113883.3.6905.2">

<displayName value="**Article 8(3) of Directive Nr. 2001/83/EC**"/>

</code>

<!-- ================================================-->

<!-- Additional information may appear after the **Application.code**, for example any-->

<!-- of the following elements related to **holder, informationRecipient,** -->

<!-- **ReviewProcedure, Application.Reference**-->

<!-- ================================================-->

<informationRecipient>

<territorialAuthority>

<governingAuthority>

<name>

<part code="**100000160750**" codeSystem="2.16.840.1.113883.3.6905.2.10" value="**NL-MEB**"/>

</name>

</governingAuthority>

</territorialAuthority>

</informationRecipient>

<subject>

<reviewProcedure>

<code code="**100000155059**" codeSystem="2.16.840.1.113883.3.6905.9" value=" **Mutual Recognition Procedure**"/>

</reviewProcedure>

</subject>

<component>

<document>

<id root="**7e72e514-4611-4229-9e19-037622a7b43a**" extension="**12345**"/>

<title value="**Pile Wonder 10mg tablets**"/>

This section needs to be repeated as often as documents need to be included, e. g. for cover letter, tracking table, variation form and PL.

<text integrityCheckAlgorithm="**SHA256**" language="**en**" charset=" **utf-8**">

<reference value="**../m1/SmPC.pdf**"/>

<integrityCheck>**3285a776897425b9a3b87abbaaf163fb261242397997b003efe3201e**</integrityCheck>

</text>

</document>

</component>

<referencedBy>

<keywordDefinition>

<code code="**FORM01**"/>

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

In case of additional keywords, this section can be repeated.

<value>

<item>

<displayName>

<translation language="**de**" value="**SmPC**"/>

</displayName>  
</item>

</value>

</keywordDefinition>

</referencedBy>

<referencedBy>

<keywordDefinition>

<code code="**FORM02**"/>

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

<value>

<item>

<displayName>

<translation language="**de**" value="**Package Leaflet**"/>

</displayName>

</item>

</value>

</keywordDefinition>

</referencedBy>

</application>

</componentOf>

</submission>

</componentOf1>

</submissionUnit>

</subject>

</controlActProcess>

</PORP\_IN000001UV>

### Managing Duplicates

In case of submitting duplicates of a new marketing authorisation application (different product names but one sponsor using the identical dossier), the assessment and processing of these duplicates can be simplified by building a group. This will be managed by the ***submissionGroup*** element. This serves as an indicator in the review system to manage all related MAAs as a group (see Section 9.17).

### Referencing across submissions and applications of the same pharmaceutical company

The principles of referencing are entirely the same, regardless of whether a reference should be presented within a Submission Unit, where a document is to be displayed with two different contexts of use, across submissions, or across applications. A ***document*** element will always be referenced by the new ***contextOfUse*** element and its ID. The ***document*** element provides the link to the PDF file. Compiler tool interoperability would require continued access to any cross application referenced documents and that they are also provided in the transfer of ownership. As a general rule, no ***document*** elements can be referenced if they are not submitted to all member states involved. In cases of MAH transfers a separate consolidating sequence might be necessary to complete the storage of competent authorities. In those cases, it is not foreseen, that document title should be changed. Changes of the document title are intended to mainly include corrections of typos. The update – mode is not considered appropriate to be used for establishing a new meaning / usage of a file. In that case a new CoU is required. From a technical point of view, the rules outlined in the ICH eCTD IG apply entirely to EU Module 1 as well.

***Note:*** *Document title corrections will be displayed wherever the document element is referenced. This effect is acceptable as no regulatory content will be changed. Further guidance as to when a document title change is allowed or recommended is provided in the ICH Implementation Guide, section on* Document Element Updates*.*

# XML MESSAGE VALIDATION RULES

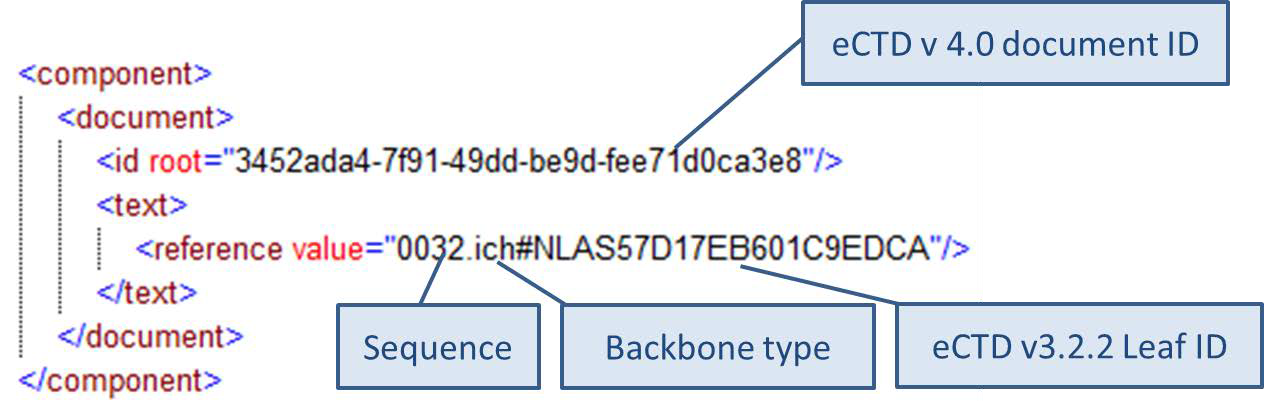
The principles of validation rules for eCTD v4.0 messages will not differ between regions. For details, please refer to the ICH Implementation Guide. The following table highlights validation rules by elements which are specifically used in the EU. Not all checks according to the schema as already mentioned in the ICH IG will be repeated here. All code / codeSystem combinations are expected to be currently valid. If an error is detected, the submission unit needs to be resubmitted including the corrected item.

|  |  |  |
| --- | --- | --- |
| **Category** | **Type/Element** | **Validation Criteria** |
| Message Validation | **Territorial** [**Authority**](#_bookmark59) | The Authority attribute must have a valid code / codeSystem combination. |
| **Submission Reference** | A Submission Unit sent by regulators must provide a Submission Reference stated as a valid code / codeSystem combination. |
| **Submission** | Submission must have a valid code / codeSystem combination. |
| **Submission Group** | Submission Group must have a valid code / codeSystem combination if it has been used.  Note: If the initial sequence of a regulatory activity makes use of the submission group element this element needs to be completed through all sequences related to that activity. |
| Submission Group id root must be a unique identifier. |
| **Mode** | Mode id root must be a unique identifier. |
| Mode code must have a valid code / codeSystem combination. |
| **Applicant** | Applicant must have a valid code / codeSystem combination. |
| Applicant status code requires the code attribute “active”. |
| **Review Procedure** | Review Procedure number must be a whole number. |
| The Review Procedure must have one and only one value for the Submission element. |
| Review Procedure for initial Submission Unit for a new marketing authorisatiuon application starts with 1. |
| **Application Reference** | Application Reference identifier is required (1..1). |
| Application Reference must have a valid code / codeSystem combination. |
| **Review** | Only one Review element can exist for a message. |
| Review code must have a valid OID for the Code System. |

|  |  |  |
| --- | --- | --- |
| **Category** | **Type/Element** | **Validation Criteria** |
|  |  | Review status code requires the code attribute “active”. |
| **Product Category** | Product Category id root must be a unique identifier. |
| Only one Product Category element can exist for a message. |
| Product Category code must have a valid OID for the Code System. |
| **Regulatory Status** | Only one Regulatory Status element can exist for a message. |
| Regulatory Status code must have a valid OID for the Code System. |

# COMPATIBILITY WITH AND REFERENCE TO PREVIOUS VERSIONS OF EU ECTD MODULE 1

The principles of forward compatibility will not differ between regions.



In case of the regional module, the backbone type will be changed into ‘eu-regional’ for the Module 1 of the EU region regardless of the specification it was built on (Version 2.0 or 3.x).

The ICH Implementation Guide describes a Forward Compatibility mechanism for conversion of a v3.2.2 application to a v4.0 message. This mechanism will enable both life cycle of active v3.2.2 content and the document re-use of v3.2.2 content, including applications that have not converted to v4.0. Detail on Forward compatibility is provided in the ICH eCTD IG Section 8.

Different from transition – forward compatibility of legacy dossiers towards version 4.0 of eCTD submissions – guidance needs to be established on how existing dossiers (not in CTD or eCTD) can be switched into eCTD once version 4.0 is implemented. Presumably, the same rules on baselining can be applied as for the switch towards eCTD v3.2.2 at the moment.

# APPENDIX 1 ABBREVIATIONS, TERMS AND DEFINITIONS

The following table defines some common terms in this document and specific to eCTD v4.0. This is not a complete listing,

|  |  |
| --- | --- |
| **Term** | **Definition** |
| **Applicant** | A pharmaceutical company or its agent that is submitting information in support of an application. |
| **Applicant’s Information** | Regulatory information submitted by an applicant for, or to maintain, a marketing authorisation that falls within the scope of this guidance document. |
| **eCTD Application** | A collection of electronic documents compiled by a pharmaceutical company or its agent in compliance with European legislation and guidelines in order to seek a marketing authorisation or any amendments thereof. An eCTD application may comprise a number of submissions and Submission Units. In the EU an eCTD application may comprise several dosage forms and strengths, all under one invented product name. This is understood to be equivalent to a Global Marketing Authorisation according to Art. 6 para 2 Dir. 2001/83/EC as amended. Some review tools describe such a collection as a dossier. |
| **Forward Compatibility** | Refers to converting v3.2.2 content into v4.0 references to achieve life cycle and document reuse. |
| **Procedure** | A Community registration procedure for the authorisation of medicinal products in the European Community. There are 4 types of procedures that operate within the EC – Centralised, Decentralised, Mutual Recognition and National. |
| **Regulatory Activity** | A collection of sequences covering the start to the end of a specific business process, e.g. an initial MA application or Type II variation. It is a concept used in some review tools to group together several business-related sequences. |
| **Submission Unit** | A single set of information and / or electronic documents supplied at one particular time by the applicant as a part of, or the complete, eCTD Application. In the context of eCTD, this is equivalent to a sequence. |
| **Document** | The ***document*** element is used for the purposes of transmitting the information about each document related to an application. Documents (e.g., PDF files) are prepared by the Applicant for review by the Regulatory Authority. |
| **Payload** | The payload is the part of [transmitted data](https://en.wikipedia.org/wiki/Data_transmission) that is the actual intended message. The payload excludes any [headers](https://en.wikipedia.org/wiki/Header_%28computing%29) or [metadata](https://en.wikipedia.org/wiki/Metadata) sent solely to facilitate payload delivery. |
| **contextOfUse (CoU)** | The Context of Use defines the relationship between the table of |

|  |  |  |
| --- | --- | --- |
|  | | contents heading (i.e., ***contextOfUse.code***) and the referenced document to be associated with that heading. The Context of Use is relevant to the sequence that it was submitted, which may include one or more ***submissions*** referenced in the ***submissionUnit***. |
| **Object** | **Identifier** | An OID is a sequence of numbers that uniquely identify an object |
| **(OID)** |  | and represent a hierarchically-assigned namespace. OIDs are |
|  |  | formally defined using the International Telecommunications |
|  |  | Union ASN.1 standard[[9]](#footnote-10). OIDs are represented as follows: |
|  |  | * String of digits separated by periods: 2.16.840.1.113883 * list of named branches: {joint-iso-itu-t(2) country(16) us(840) organisation(1) hl7(113883)} |
|  |  | The current OIDs for the ICH domain include: |
|  |  | * ich-estri – 2.16.840.1.113883.3.989 * ich-estri-msg-stds – 2.16.840.1.113883.3.989.2 * ich-estri-msg-stds-m8-ectd – 2.16.840.1.113883.3.989.2.2 * ich-estri-msg-stds-m8-ectd-code-lists – 2.16.840.1.113883.3.989.2.2.1 * ich-estri-msg-stds-m8-ectd-code-list-valueset-version – 2.16.840.1.113883.3.989.2.2.1.x.y |
| **Universal Unique Identifier (UUID)** | | A UUID is hexadecimal text in the form of 8-4-4-4-12 characters, i.e., text value includes 32 characters and 4 hyphens[[10]](#footnote-11). UUIDs are formally defined by ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005. UUIDs are represented as follows:   * String of digits separated by hyphens: 25635f23-a3a4- 4ce0-9994-99c5f074960f   In ICH eCTD v4.0, UUIDs will be used for any identifier root attribute value. Each required element with an identifier (e.g., ***id*** element) will indicate when a UUID should be provided |

1. The ICH IG is accessible at [www.estri.org](http://www.estri.org/) [↑](#footnote-ref-2)
2. The regional implementation agreed for the EU will apply in the same way to the EEA countries Iceland, Norway and Lichtenstein, according to the general agreement in regard to the legislation on medicinal products. [↑](#footnote-ref-3)
3. The term ‘dossier’ is understood as the eCTD application covering several dosage forms and strengths all under one invented product name (see also Appendix 1 Glossary). Both terms will be used synonymously. [↑](#footnote-ref-4)
4. The ICH IG is accessible at www.estri.org [↑](#footnote-ref-5)
5. A complete package for implementation is provided at [www.estri.org.](http://www.estri.org/) [↑](#footnote-ref-6)
6. Controlled vocabularies (aka Referentials) are lists of terms that refer to attributes of the medicinal and the pharmaceutical product e.g. dosage form, route of administration, unit of measurement. The SPOR data services will cover Substance Management Services (SMS), Product Management Services (PMS), Organisations Management Services (OMS), and Referentials Management Services (RMS). Based on terms in RMS for controlled vocabularies used specifically for eCTD v4.0 messages, the following OID is proposed instead to provide the required lists in a more practical format (genericode) and constrained according to need: 2.16.840.1.113883.3.6905.2 and will have several child OIDs, e.g. 2.16.840.1.113883.3.6905.2.1([Applicants Submission Unit Type](http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155046&firstTime=true&d-5037238-p=1&d-5037238-n=1&d-5037238-o=1&d-5037238-s=termName)), 2.16.840.1.113883.3.6905.2.4([Application SubmissionType](http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155688&firstTime=true&d-5037238-p=1&d-5037238-n=1&d-5037238-o=1&d-5037238-s=termName)), 2.16.840.1.113883.3.6905.2.6([eCTD EU Context of Use](http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155719&firstTime=true&d-5037238-p=1&d-5037238-n=1&d-5037238-o=1&d-5037238-s=termName)) (see Table 3: Controlled Vocabularies for EU purpose in Section 6.1). [↑](#footnote-ref-7)
7. The Referentials Management Service (RMS) can be accessed at <https://spor.ema.europa.eu/sporwi/> . The machine readable constrained list of controlled vocabulary lists is available at <http://esubmission.ema.europa.eu>. [↑](#footnote-ref-8)
8. The previous EUTCT is replaced by the Referentials Managemet Services (RMS). [↑](#footnote-ref-9)
9. International Telecommunication Union, x680: Information technology – Abstract Syntax Notation One (ASN.1): Specification of basic notation [↑](#footnote-ref-10)
10. 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 [↑](#footnote-ref-11)