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

Draft for Public Consultation

Version 2.0
March 10th, 2015

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  *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 Chap 1 to 5, mostly editorial changes
1.05	21st Jan 2015	Consolidating comments and text improvements of

		Chap 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 top 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

TABLE OF CONTENTS Page

LIST OF FIGURES

LIST OF TABLES

NOTICE TO READER

Sections of this document referencing the HL7 (Version 3) Standard: 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.

1. 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 Regulated Product Submission (RPS) Release 2 Normative. Applicable Information indicated in the ICH eCTD IG[1] 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.

Note to Implementers: This EU Module 1 IG will need to be used in conjunction with the ICH eCTD IG, as the eCTD v4.0 message will be incomplete without all of the contents.

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 ruled out 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 and/or differently from common CTD Modules 2 – 5.

The content of eCTD v4.0 Modules 2 - 5, being shared across all ICH regions, is not included in this IG, although some principles need to be repeated to assure a better understanding. This document 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.

2. Background

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 regarded as the principal electronic submission format in the EU[2] and is the only electronic format that is accepted by the European Medicines Agency (hereafter referred to as EMA) and presumably all National Competent Authorities (hereafter referred to as NCAs).

[1] The ICH IG is accessible at www.estri.org

[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.

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 enhance significantly 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 'contents of use' which will allow one piece of data to be used across many applications, avoiding the need for duplication of data elements. More details can be found in Section 4.3 of this document as well as in the ICH eCTD IG.

3. CHANGE CONTROL RULES

Change requests need to be addressed to the relevant organisation which is responsible for the part the standard or the implementation is based on:
eCTD v4.0 is based on the HL7 Regulated Product Submission (RPS) Message Standard Version 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 rules outlined at HL7.
Changes to the ICH eCTD v4.0 IG and ICH Controlled Vocabularies remain the responsibility of the ICH M8 Expert Working Group (EWG) and will follow the established eCTD change control process.
In a situation where EU M1 IG need 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, an Electronic Submission Change Request/Q&A Form -should be provided and this can be found at http://esubmission.ema.europa.eu/doc/index.html.

4. ESSENTIAL COMPONENTS OF THE ECTD IN CONSIDERATION OFTHE 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:

- Object Identifier (OIDs) and Universal Unique Identifier (UUIDs) (further information provided in the ICH eCTD IG, Section 4.5)
- Data Types (further information provided in the ICH eCTD IG, Section 4.6)
- Files and Folders (see Section 5 of this document, further information provided in the ICH eCTD IG, Section 5 and Section 11)
- Controlled Vocabulary (see Section 6 of this document, further information provided in the ICH eCTD IG, Section 6)

- ICH eCTD v4.0 XML Schema (further information provided in the ICH eCTD IG, Section 7)
- eCTD v4.0 XML Message (see Section 8 of this document, further information provided in the ICH eCTD IG, Section 8)
- Validation Rules (see Section 11 of this document, further information provided in the ICH eCTD IG, Section 12)
- Forward Compatibility (see Section 12 of this document, further information provided in the ICH eCTD IG, Section 10)

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

- ICH eCTD IG across regions (separate document[3])
- EU Module1 IG regionally (this document).

Therefore, in order to compose a complete eCTD v4.0 compliant message, the the user needs to refer to the requisite documentation published by ICH[4].

4.1 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***
  - ***subject8.reviewProcedure***
  - ***reference.applicationReference***
  - ***holder.applicant***
  - ***informationRecipient.territorialAuthority***
- ***submission***
  - ***subject3.regulatoryReviewTime***
  - ***subject4.submissionGroup***
  - ***subject5.mode***
- ***review***
  - ***subject1.manufacturedProduct***
  - ***subject2.productCategory***
  - ***subject3.regulatoryStatus***
  - ***holder.applicant***
  - ***author.territorialAuthority***

For EU Module 1 the following elements are excluded

[3] The document will be accessible at www.estri.org

[4] A complete package for implementation will be provided at www.estri.org once the Step 4 of the acknowlegdement process has been reached.

- ***categoryEvent***
  - ***categoryEvent***
- ***submission***
  - ***subject6.regulatoryReviewTime***

4.2 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).
- **Submission Units with Multiple Submission components** (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 10.3 of this document).
- **Two-way Communication** – includes information on Regulatory Authority communication with the Applicant (see Section 10.4 of this document).

4.3 Major Changes and Advantages of eCTD v4.0

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

- Options to accomodate regulatory changes without delay and major technical changes
- Simplification of life cycle
- Flexibility of dossier granularity and grouping of documents
- Assigning submission units to different applications by only referencing a sequence number and application ID
- Referencing documents across applications
- Two way communication
- Applicability to all kind of products

5. SUBMISSION CONTENTS, FOLDER AND FILE STRUCTURE

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

The ICH Common Technical Document ("CTD") specifies that Module 1 should contain region-specific administrative and product information. The content and numbering of Module 1 for the EU is detailed in the latest version of the *Notice to Applicants* that can be found at:
http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm

The following items listed in the Notice to Applicants should be included in an initial application submission unit

- cover letter,
- comprehensive table of contents[5],
- application form,
- product information documents,
- information on the experts,
- specific requirements for different types of applications (if required),
- environmental risk assessment,
- information relating to orphan market exclusivity (if required),
- information relating to pharmacovigilance,
- information relating to clinical trials (if required),
- information relating to paediatrics.

In addition, other items as applicable including nationally required information, answers to regulatory questions, rationale for variations and renewal documentation should also be included in Module 1.

Whenever regulators use the eCTD v4.0 message for sending assessment reports, lists of questions or lists of outstanding issues to applicants, these types of submission units will become contained within Module 1 of the applicable application.

It should be noted, that for subsequent submissions in the lifecycle of a medicinal product, e.g. for a variation, not all of the above mentioned types of documents need be included in Module 1. Consult the various legal documents for guidance on the exact documents to be submitted in such cases, e.g. Regulation Guidance for Type IA, Type IB and Type II variations as well as respective business guidance documents.

5.1 Submission Unit Content

The submission unit consist 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", and 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.

[5] TOC not required for eCTD as the XML message acts as a table of contents

- Files previously sent do not need to be sent again.
- It is possible to reference documents across applications (equivalent to the term dossier)

5.2 Naming Conventions

The naming conventions for folders for EU Module 1 will remain the same as in previous versions of the eCTD. eCTD v4.0 enables the applicant to omitt the additional folder level for language or country-specific documents. This will be replaced by using keywords from the respective controlled vocabulary (see Section 6.3), which is also required for selective display of information. Aside from this change the EU Module 1 folder structure will remain the same.

Additional guidance for naming conventions on folders is provided in the ICH eCTD IG and will be applicable commonly.

5.2.1 Allowable Characters

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

5.2.2 Length of Names and the Path

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

5.3 Top Folder Naming Requirements

In **general**, to identify the content with a folder structure e.g. when on portable electronic media or after extracting compressed content from a container, the top folder must be named according to the main part of the application procedure number relating to the regulatory. Below are examples, e.g.

- **de2087** or **uk3456** in case of the MR/DC procedure (e.g. DE/H/2087/001/MR or UK/H/3456/001-005/DC respectively),
- **2131577** 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 case of **grouping or worksharing** regulatory activities including PSUR worksharing and single assessment procedures the top folder naming needs to reflect the procedures type more specifically, e.g.

- **de0001g** or **uk0019g respectively es0002ws or fi 0005ws** in case of the grouping where DE or UK respectively ES or FI are the RMS and the first or nineteenth grouping respectively the second or fifth worksharing for national procedures across some member states is submitted.,
- **se1234psur** in case of a PSUR worksharing where SE is RMS (The number will be taken from the EURD list).,

- **ema0011g or ema0009ws** in case a centrally authorized product is involved in the worksharing.
- **PSUSA00002172** in case of EU PSUR Single Assesment Procedure e.g. PSUSA/00002172/2015
-

In these cases a short life cycle will be established referencing the documentation to all applications involved. Thereby an URL can be established to the physical storage area where the submission units will be archived.

5.4 Second Level Folder Naming Requirements

In **general**, for the second level folder name, the sequence number will be used.

For **grouping or worksharing** regulatory activities, several sequences can be included in the submission unit;, the second level folder name should be in the format of 999900. For additional submission units related to this regulatory activity the second level folder name will be take the form, 999901, 999902 etc. This second level folder naming convention will be used for all subsequent groupings or worksharing activities along the life cycle of the the products (applications).

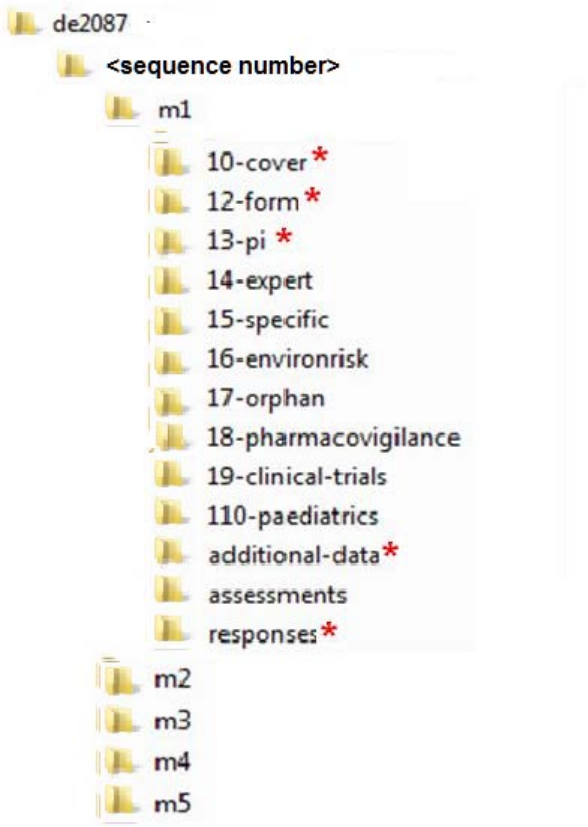
5.5 Pathname Conventions and Best Practices

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

5.6 Folder Hierarchy

To comply with the naming and pathname conventions outlined above, the actual physical structure of the folder hierarchy will be the following (Figure 1):

Figure 1: Folder Hierarchy of Module 1 Screenshot



* *In these folders the CC- or LL-folder are no longer required. Instead, keywords must to be applied for country at contextOfUse level. Controlled terms will be introduced at document level to specify the document type. Language is included as attribute of the document element.*

5.7 File Formats

In general, for messages to competent authorities in the EU [6] the ICH M2 recommendations on file format [7] and the specification for submission formats [8] of ICH M8 need to considered. However in the EU Module 1 files of formats as detailed below are acceptable:

Table 1: Acceptable file formats for Module 1

Document	File Format	Remark
Cover letter	PDF*	PDF preferably generated from electronic source.
Administrative forms: • Application form and its annexes • Variation application form incl. background for the variation • Renewal form and its annexes	XML*, PDF XML, PDF XML, PDF	Documents should be generated from electronic source documents, any signature may be embedded as a graphic file in the PDF text if desired, although this is not always necessary depending from the receiving agency. Currently, there is no common position adopted by the regulatory network in regard to signatures in PDF documents.
Product Information: • Product information text*** • Packaging mock-ups • Reference to specimens	 PDF PDF PDF	If a higher resolution is necessary for the mock-ups, use JPEG, GIF, PNG or SVG on a case-by-case basis.
Other	PDF	PDF preferably generated from electronic source.

* PDF = Additional details on PDF and PDF/A formats can be found in ICH M2 recommendations.

** = 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).

*** = SmPC, Package Leaflet and labelling

5.8 Checksums

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

[6] 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.

[7] http://estri.org/recommendations/index.htm

[8] http://estri.org/new-eCTD/index.htm

6. CONTROLLED VOCABULARIES

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 terminology – i.e., the controlled vocabulary determined by ICH are stated in the ICH Implementation Guide.

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.*
- *During Step 2, the controlled vocabulary will be provided using OID assigned specifically. All EU regionally required controlled terms are available at http://eutct.ema.europa.eu/eutct/displayWelcome.do.*

6.1 Keywords and Controlled Vocabularies for EU Purpose

Keywords need 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 for documents in “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 a product information text is dedicated for. These user defined keywords should be used for Module 3 purpose at the same time.

Note to Implementers: *The previously required language folder in “13-pi” will be replaced by documentLanguage.code (see:* Section 9.7*)*

The controlled vocabularies specified for the EU Module 1 part of the eCTD v4.0 message are provided below with a brief description of the terminology and location for obtaining detailed information.

316

Table 2: Controlled Vocabularies for EU purpose

CV list name	Purpose	Source
Context of Use Codes	Examples of enhancement features and the re-use of data are in the contents of use which will allow one piece of data to be used across many applications, avoiding the need for duplication of data elements. More details can be found in the ICH Implementation Guide.	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155719
Keyword Definition Codes	Keyword codes for the type of keywords that are defined by the keywordDefinition CTD structure for EU Module 1	Will apply to document type (see Document Type Code), language, country (see Section 6.3)
Application Codes	Type of application the product can be categorised	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000000012
Application Reference Reason Codes	Reasons, for which a reference to an already authorised medicinal product is used, e.g. in case of a generic product	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000154440
Contact Party Codes	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	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000154441
Document Type Codes	Type of keyword that is applied to a product information document. This Controlled Term List contains the types of product information documents, which are part of the eCTD Module 1.3.1	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155531
Mode Codes	Indicate whether the regulatory activity will be handled as a group or in a single or work shared manner	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155533
Ingredient Role Codes	Role of each of the ingredients in the composition of a medicinal product	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000072050
Manufactured Product Codes	Type of the product under review based on the pharmaceutical form	http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/03/WC500123648.xls
Product Category Codes	Type of the 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	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155526
Substance Codes	Used to name the ingredient based on its role of an active ingredients. The	http://www.ema.europa.eu/docs/en_GB/docume

	proposed EUTCT Controlled Term List ID is 100000072072.	nt_library/Other/2013/04/WC500142231.xlsx
Place Codes	Used to name the territorial area for which the competent authority's decision will apply to	This is a subset of the EEA country codes derived from the ISO two letter country code list (see Section 6. 3)
Regulatory Status Codes	Status of the review of a regulatory activity	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000072049
Review Procedure Codes	Type of regulatory authorisation procedure in the European Union	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000154442
Submission Codes	Type of regulatory activity constituted by one or several submission units and referring to at least one application	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155688
Applicant's submission unit type Codes	Types of content of submission unit items to be provided by an applicant	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155046
Regulating Authority's submission unit type Codes	Types of content of submission items to be provided by a regulating Authority	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000155552
EU Procedural Authority Role Codes	Role of a regulating party involved in a regulatory activity depending from the procedure type	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=
Territorial Authority Codes	Competent Authorities responsible for Medicinal Product authorisation in the European Union and the European Economic Area, including name of the country and its domain of expertise. In case of eCTD the usage is restricted to Competent Authorities responsible for human medicinal products.	http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000160680

6.2 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 Module 2 to 5, see ICH eCTD IG for details.

6.3 Controlled Vocabulary specified by ISO

The controlled vocabulary specified by other organisations (i.e., not managed by ICH, Region or HL7) are provided below noting 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 EUTCT).
- **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 used.
- **ISO Health informatics – Identification of Medicinal Products – Structures and Controlled Vocabularies** for *Ingredients (Substances)* (prEN ISO 11238).

6.4 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 EUTCT for the purpose of EU Module 1 use.

7. eCTD v4.0 XML Schema

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

8. eCTD 4.0 XML Message

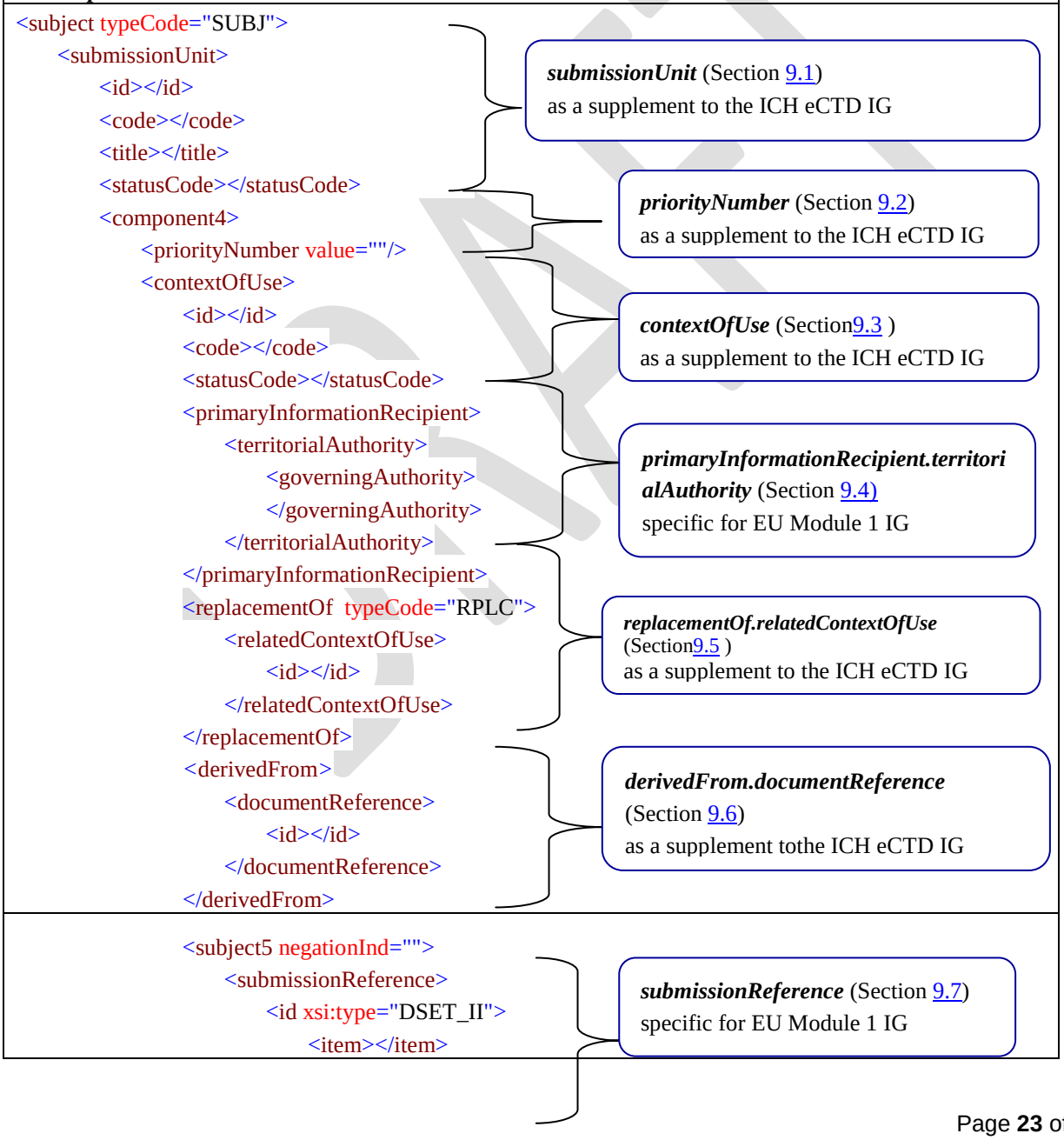
There are no principles deviating from the ICH Implementation Guide for creating the EU part of the XML message. Especially, in regard to the header of the message the same elements/attributes apply as outlined in the ICH eCTD IG. Nevertheless, additional regional specific requirements need to be considered for other elements/attributes as outlined below.

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

361

Table 3: XML Structure

XML Structure
The eCTD v4.0 begins by identifying the ***subject*** element of the XML message. The payload message starts with the ***submissionUnit*** element and relates the rest of the elements to the Submission Unit being sent. The ***submissionUnit*** element contains the following elements and their attributes: • ***component4contextOfUse*** o ***priorityNumber*** o ***replacementOf.relatedContextOfUse*** o ***derivedFrom.documentReference*** o ***subject5.submissionReference*** o ***referencedBy.keyword*** o ***primaryInformationRecipient.TerritorialAuthority*** • ***component1.submisison***



XML Structure

```
                    </id>
                </submissionReference>
            </subject5>
            <reference1 typeCode="REFR">
                <keyword>
                    <code></code>
                </keyword>
            </reference1>
        </contextOfUse>
    </component4>
```

Keyword (Section 9.8)
as a supplement to the ICH eCTD IG and specific for EU Module 1 IG

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***)
- ***callBackContact.contactParty***
- ***subject4.review***
- ***subject6.regulatoryReviewTime***
- ***subject7.submissionGroup***
- ***subject9.mode***

```
        <component1>
            <sequenceNumber></sequenceNumber>
            <submission>
                <id></id>
                <code></code>
                <callBackContact>
                    <contactParty>
                        <id></id>
                    </contactParty>
                </callBackContact>
                <subject4>
                    <review>
                        <….>
                        /<….>
                    </review>
                </subject4>
                <subject6>
                    <regulatoryReviewTime>
                        <code></code>
                    </regulatoryReviewTime>
                </subject6>
                <subject7>
                    <submissionGroup>
                        <id></id>
                    </submissionGroup>
                </subject7>
                <subject9>
                    <mode>
                        <code></code>
                    </mode>
                </subject9>
```

sequenceNumber.submission (Section 9.9)
as a supplement to the ICH eCTD IG

submission (Section 9.10)
specific for EU Module 1 IG

callBackContact (Section 9.11)
specific for EU Module 1 IG

review (Section 9.22)
see separate section below

regulatoryReviewTime (Section 9.12)
not required

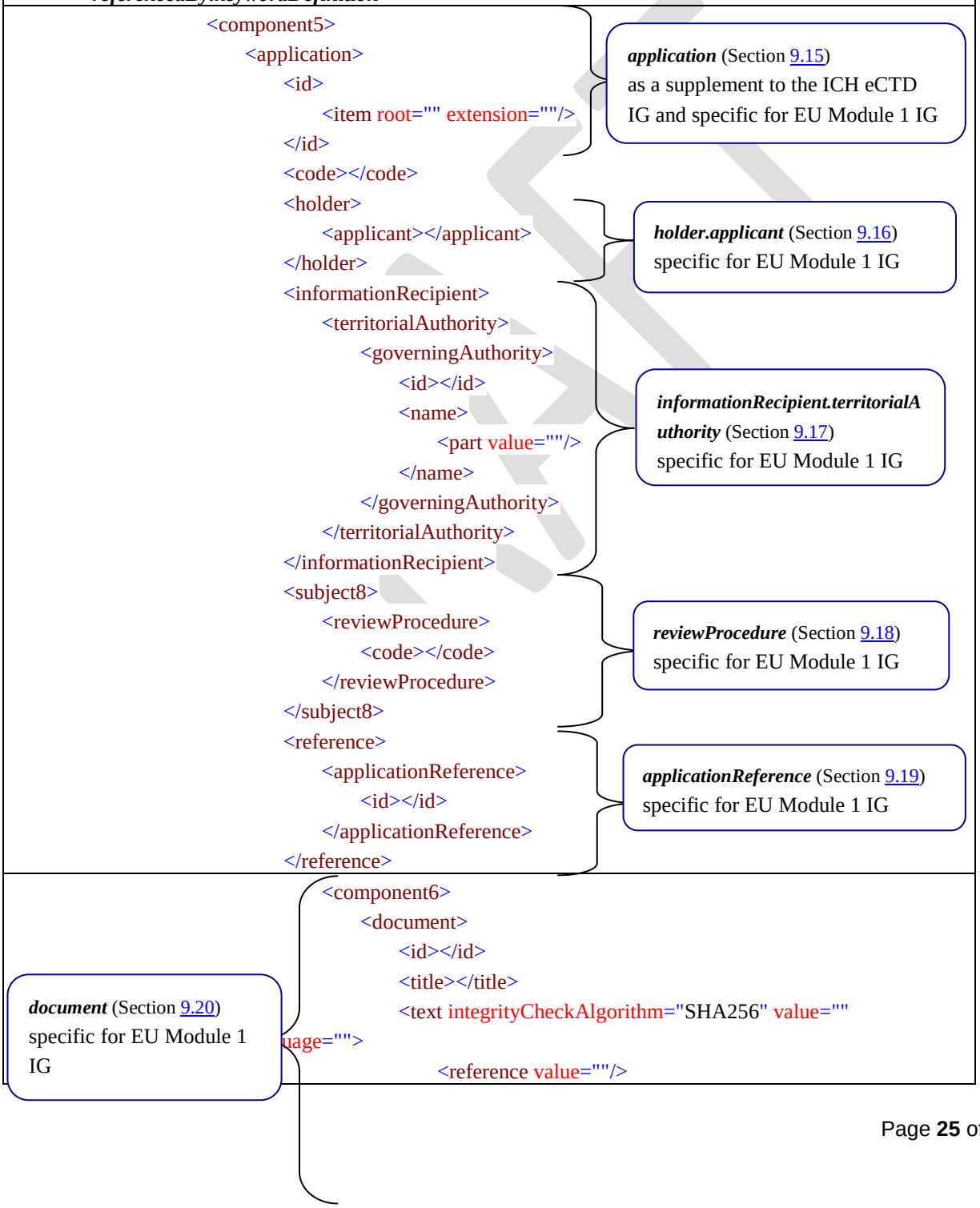
submissionGroup (Section 9.13)
specific for EU Module 1 IG

mode (Section 9.14)
specific for EU Module 1 IG

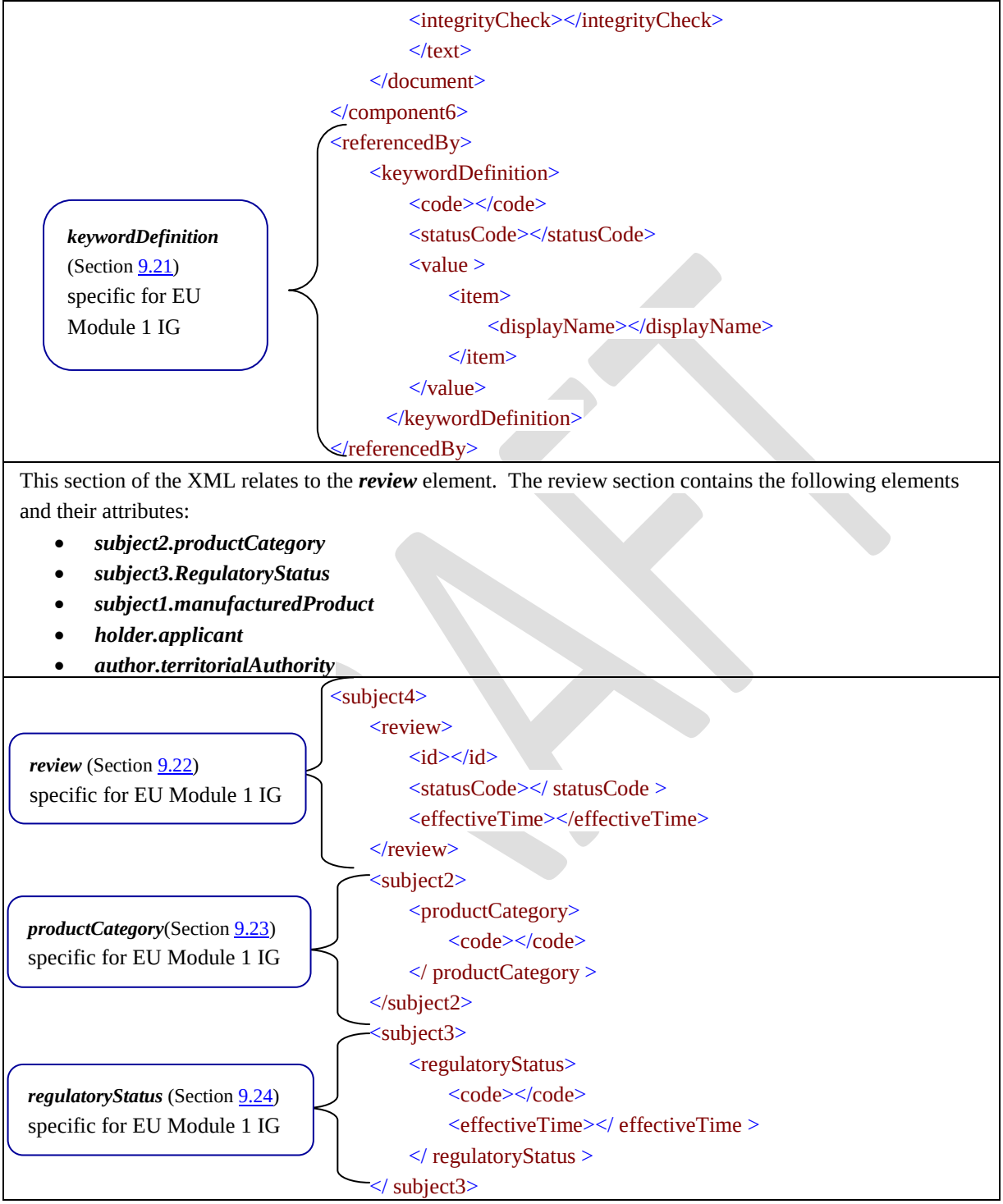
XML Structure

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

- ***holder.applicant***
- ***informationRecipient.territorialAuthority***
- ***subject8.reviewProcedure***
- ***reference.applicationReference***
- ***component6.document***
  - ***referencedBy.keyword***
- ***referencedBy.keywordDefinition***



XML Structure

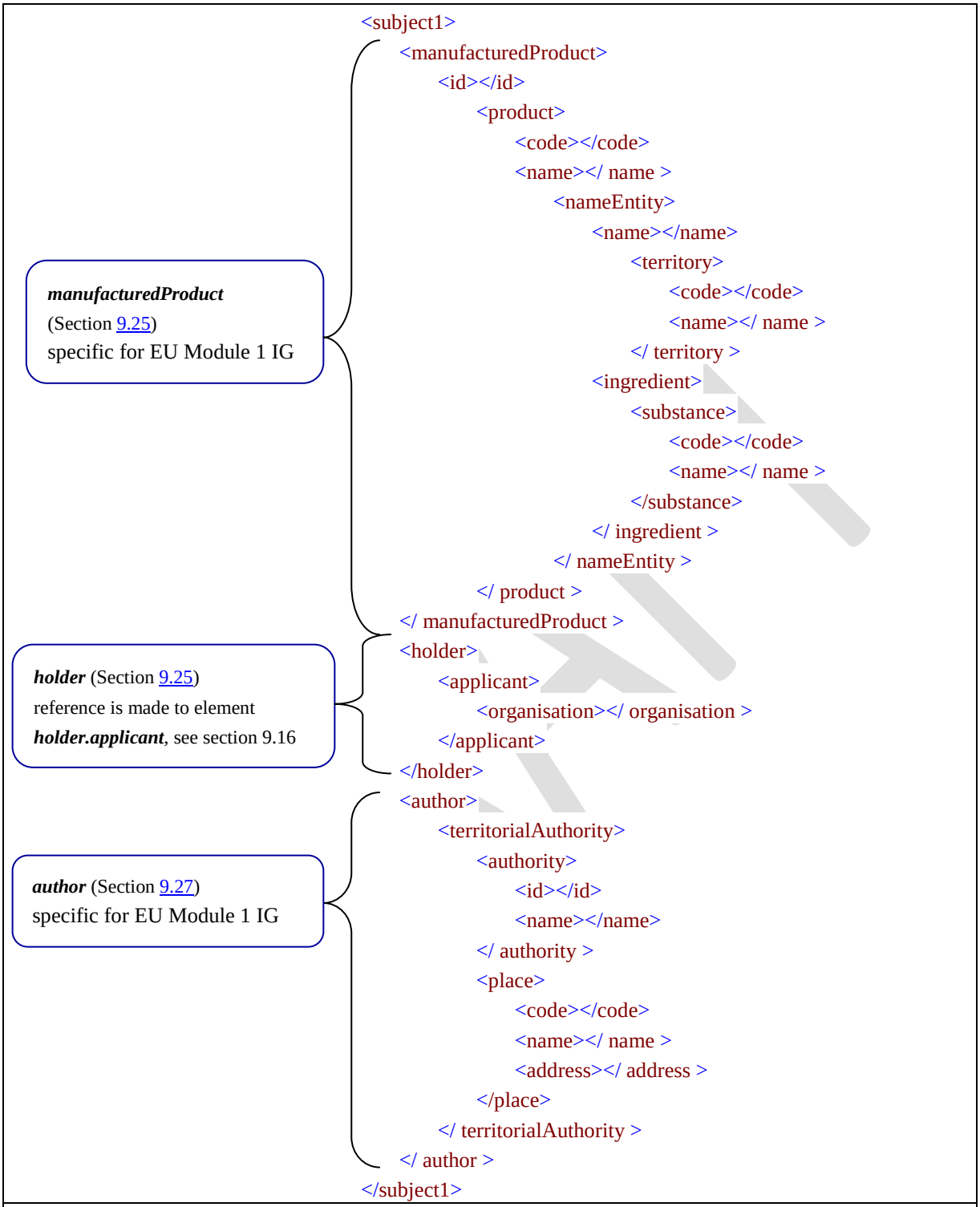


This section of the XML relates to the ***review*** element. The review section contains the following elements and their attributes:

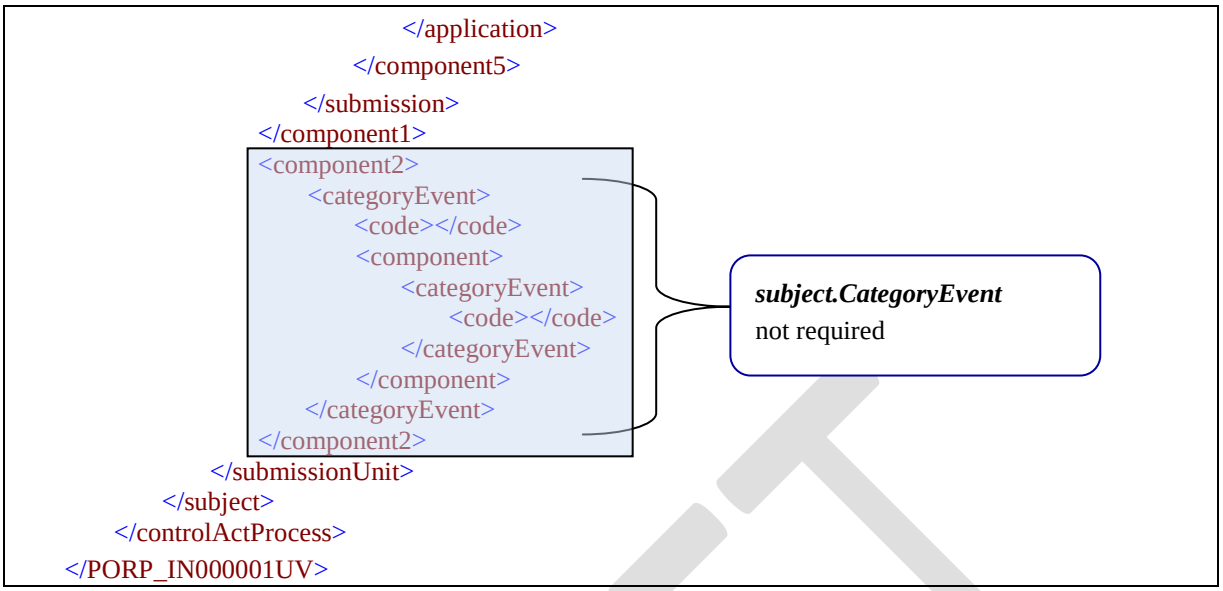
- ***subject2.productCategory***
- ***subject3.RegulatoryStatus***
- ***subject1.manufacturedProduct***
- ***holder.applicant***
- ***author.territorialAuthority***

362

363



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***).



9. EU REGIONAL SPECIFIC REQUIREMENTS FOR ELEMENTS

9.1 Submission Unit

The Submission Unit is a collection of documents provided to the Regulatory Authority at one time or to the Applicant in case the Regulatory Authority will send their list of question or assessment report using the same messaging standard. 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, this 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.

In case of regulatory activities executed in a grouping or workshare mode, the submission unit will be referenced for multiple applications as needed through a submission element each time providing the respective sequence number. The submission element connects the submission unit and the application.

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

9.1.1 Location in XML

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

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

Refer to Table 3: XML Structure for the XML representation.

9.1.2 XML details

There are no additional requirements than 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 here. 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="78965412-3214-5698-7856-985412563254"/>
       <code code=" Applicant's submission unit type " codeSystem="12365478-9874-5632-
11235-951268473654"/>
       <title="initial" codeSystem="12311898-4574-5122-99435-94321434564"/>
      <statusCode code="active"/>
          ……
            [Additional information may appear after the addition of the statusCode (if one exists,
            otherwise this will follow 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, callBackContact, componentOf or subject elements]
           …
      <component1>
         <sequenceNumber value="1"/>
         <submission>
         …
           [Additional information will follow for the submission and application elements.]
         …
         </submission>
      </component1>
    </submissionUnit>
</subject>
```

9.2 Priority Number

There are no additional requirements than 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.

9.3 Context of Use

The Context of Use provides a linkage between the table of contents heading of the CTD and the referenced document that is associated to that heading. There are no additional technical requirements than 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.

9.3.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component4>>priorityNumber> contextOfUse***

Refer to Table 3: XML Structure for the XML representation.

9.3.2 XML Details

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

9.3.3 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.

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

The elements ***primaryInformationRecipient*** and ***informationRecipient*** (see Section 9.17) will provide names of ***territorialAuthority***. For Centralised procedure this does mean the EMA will be stated in both cases. In case of DCP the Reference Member State, i.e. France, will be named by using the ***primaryInformationRecipient*** element and the ***informationRecipient*** element, all Member States involved, i.e. The Netherlands, France, Germany (BfArM), will be named by using only the ***informationRecipient*** element. This element will be provided once as always only one agency will serve as a primary recipient.

9.4.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component4>> contextOfUse>>primaryInformationRecipient>>territorialAuthority***

Refer to Table 3: XML Structure for the XML representation.

9.4.2 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 "TERR". This value is not required in the XML message.*

TerritorrialAuthority.place

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
id		[1..1]		This is a container element for a reference to the place of the governing authority
id.item		[1..1]		The ***place*** attribute of the ***territory*** element provides the physical location of the territorial authority (e.g., regulatory authority) for which the respective agency is responsible for
	code	[1..1]	Alpha Numeric e.g., DE	The code will be provided by the EU Territorial Authority Code list
	root	[1..1]	Valid OID or UUID	

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
	name	[0..1]	Alpha Numeric e.g., Germany	The ***name*** element will display the name of the country / territory
	address	[0..1]	Alpha Numeric e.g., Kurt-Georg-Kiesinger-Allee 3; 53175 Bonn	The ***address*** element will provide the display value of address details of the respective authority
Conformance	The ***id*** element and ***root*** attribute are required.			
Business Rules	This element provides the referencing point for the competent authority responsible for the assessment procedure and indicates for whichterritory the respective agency is responsible 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***			

475

476

477 ***TerritorrialAuthority.governingAuthority***

Element	Attribute	Cardinality	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		[1..*]		This is the container element of the following attributes by which the name of the regulating authority is provided.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
	code	[1..1]	Alpha Numeric e.g., BfArM or 276	The ***code*** element will provide the unique identifier of the authority
	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.*
	name	[1..1]	Alpha Numeric e.g., Bundesinstitut für Arzneimittel und Medizinprodukte	The ***name*** element will display the name of the authority
Conformance	The ***id*** element and ***root*** attribute are required.			
Business Rules	This element provides the referencing point for the competent agency receiving the message as a primary recipient, e.g. the EMA in case of a Centralised procedure, the RMS in DCP or MRP or the respective NCA in case of a purely national procedure.			
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

```
<primaryInformationRecipient>
<!-- Specific Health Authority and/or country to which this CoU is for (if needed to be
specified) -->
  <territorialAuthority>
```

```
    <territory>
      <code code="FR" codeSystem="4.33.650.1.723354.0.121.230" />
      <name>
        <part value = "National Agency for the Safety of Medicine and Health Products"
language="en"/>
      </name>
      <addr xsi:type="AD">
      <part value="Saint-Denis" type="CTY" />
      <part value="143-147 Bld Anatole France" type="STR"/>
      <part value="93200" type="ZIP" />
      </addr>
    </territory>
    <governingAuthority>
      <id root="52345678-1234-1234-1234-12345678901" />
      <name>
        <part value="ANSM" code="FR-ANSM" />
      </name>
    </governingAuthority>
  </territorialAuthority>
</primaryInformationRecipient>
```

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

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

9.6 Document Reference

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

9.7 Submission Reference

The Submission Reference provides the option to refer to a submission sent by applicant in case the authority will use two-way communication. The ***submissionReference*** element indicates the previously started regulatory activity to which the authority response relates. The ***submissionReference*** element will be used by regulators only.

9.7.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component4>> contextOfUse>>subject5>>submissionReference***

Refer to Table 3: XML Structure for the XML representation.

9.7.2 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***
	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			
Business Rules	More than one ***item*** element may be provided.			

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***			

535

536

537 ***XMLSample: Submission Reference***

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

539

Note: Examples for XML snippets will be provided in one of the future versions

540

See XML Color Legend for color usage

541

542 ### 9.7.3 Terminology

543 There is no further terminology foreseen.

544

545

546 ## 9.8 Keyword

547 The ***keyword*** element is used for the purposes of transmitting additional information about a
548 ***contextOfUse*** element. In the EU M1, the Country Code will be used to specify commonly used
549 or nationally used documents including the referenced files. The keywords to identify types of
550 product information texts will be used for ***contextOfUse*** elements related to Module 1.3.1.

551 The ***keyword*** is either defined by an external controlled vocabulary, e.g. Document Type Code,
552 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.

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.

9.8.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component4>>priorityNumber> contextOfUse >> reference1>> keyword***

Refer to Table 3: XML Structure for the XML representation.

9.8.2 XML Details

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

9.8.3 Terminology

For EU Module 1 controlled vocabularies are provided via EUTCT (see Section 6.1).

9.9 Sequence Number

There are no additional requirements than outlined in the ICH eCTD IG. In case more than one sequence number need to be provided (in case of grouped variations and work share procedures) the sequence number needs to be stated as required next to the application involved in the grouping or work shared procedure.

9.10 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. However, for the purposes of the Current View Transition message the ICH Controlled Vocabulary should be used.

A submission unit may contain more than one submission referring each to one application (see Section 5), relevant in case of grouped variations or workshare procedures.

Remark: The id@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.

9.10.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> sequenceNumber>>submission***

Refer to Table 3: XML Structure for the XML representation.

9.10.2 XML Details

The following attributes are used with the ***submission*** element:

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
	extension	[1..n]	alpha-numeric e.g. DE/H/1234/001-003/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.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
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***			

595

596 ***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.			
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 6.1.18.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
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***			

597

598 ***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***			

599
600

XML samples:

Submission

Note: Examples for XML snippets will be provided in one of the future versions

Submission componentOf Application

Note: Examples for XML snippets will be provided in one of the future versions

See XML Color Legend for color usage

9.10.3 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.

9.10.4 Related Elements

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

- ***subject4.review*** (see Section 9.22)
- ***subject6.regulatoryReviewTime*** (see Section 9.12)
- ***subject7.submissionGroup*** (see Section 9.13)
- ***subject9.mode*** (see Section 9.14)

9.11 Contact Party

The ***callBackContact*** element is to be used for a person or department (***contactParty***) to call 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)

In case of the Transition Mapping submission file a technical contact party should be included for the purposes of troubleshooting any issues with the forward compatibility file. The following information should be sent for each technical contact.

9.11.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>callBackContact>>contactParty***

Refer to Table 3: XML Structure for the XML representation.

9.11.2 XML details

There are no additional requirements than outlined in the ICH eCTD IG. The sample provided there is applicable for other contact party roles as well.

9.11.3 Terminology

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

9.12 Regulatory Review Time

The ***regulatoryReviewTime*** element element will not be used in the EU.

This class will not be used in EU Module 1 eCTD v4.0 message, because the review time is already defined by legislation and does not need to be stated in the message.

9.13 Submission Group

The Submission Group represents an option to process regulatory activities together in case the assessment will cover same content and the regulatory activity concerns more than one variation for the same product or applies to more than one product, e.g several generic applications with different product names but identical pharmaceutical composition and properties which can otherwise not be assessed like grouped variations or other formal workshare procedures in one go. 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 in case same regulatory activity will be processed the same way but formally not running under the same procedure number or can be grouped or shared according legal rules. The UUID will connect the different applications for this submission (regulatory activity) in the submission group, e.g. id=0987.997.

9.13.1 Location in XML

The ***submissionGroup*** element follows the ***submission*** element, which follows the ***subjectOf*** element.

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

- ***controlActProcess>> subject>> submissionUnit>>componen1>> sequenceNumber>>submission>>subject7>>submissionGroup***

Refer to Table 3: XML Structure for the XML representation.

9.13.2 XML details

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

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 of which the submission is part of
id.item		[1..*]		This is the container element of the following attributes by which it uniquely identifies the referenced submission.
	root	[1..1]	Valid UUID	The ***root*** attribute of the ***id*** element provides a global unique identifier for the submission reference.
Conformance	The ***id.item@root*** is a required attribute.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Business Rules	More than one ***item*** element may be provided. This will indicate a group of applications the regulatory activity applies to but not formally as a grouping or worksharing, but in case of duplcates processed together but as independent produucts.			
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***			

XML Sample: SubmissionGroup derived from Submission

```
<subject7>
   <submissionGroup>
      <idroot="UUID for the submissionGroup" extension="0987.997" />
   </submissionGroup>
</subject7>
<componentOf>
   <application>
      <id>
      - <!-- Application ID -->
      - <!-- ============ -->
      - <!-- Should EU use this item to store the number used by an agency to track the
submission, in any procedure, in relation to a particular product. -->
      - <!-- This could be a MRP Number, the EMEA application number, or any other number
used by an agency to track a submission. -->
      - <!-- ============ -->
         <item root="fr-2082-001-dc" />
         <item root="fr-2083-001-dc" />
         <item root="fr-2084-001-dc" />
         <item root="fr-2085-001-dc" />
      </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>
```

See XML Color Legend for color usage

9.13.3 Terminology

There is no further terminology foreseen.

9.14 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 line 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 or a PSUR single assessment procedure) and an activity subject to a worksharing agreement (e.g. a Type II variation applicable to more than one marketing authorisation).

9.14.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> sequenceNumber>>submission>>subject9>>mode***

Refer to Table 3: XML Structure for the XML representation.

9.14.2 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*** is a required element			
Business Rules	If the mode element is been used the code is required as well.			
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***code@codeSystemName*** • ***code@codeSystemVersion*** • ***code@valueSet*** • ***code@valueSetVersion*** • ***code@originalText*** • ***code@codingRationale*** • ***code@translation*** • ***code@source***			

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

XML Sample : Mode

```
<componentOf>
  <sequenceNumber value="2" />
  <submission>
```

```
    <id>
      <item root="0F7650B5-F126-424C-8AC6-75E11B08C202" />
    </id>
    <code code="100000155689" codeSystem="9.16.330.1.113884.2.800.2"/>
    <subject9>
      <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 -->
        <code code="worksharing" codeSystem="3.12.850.1.223354.0.121.1" />
      </mode>
    </subject9>
          ...
            [Additional information may appear]
          ...
  </submission>
</componentOf>
```

See XML Color Legend for color usage

9.14.3 Terminology

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

9.15 Application

The a***pplication*** element represents a request from Regulated Industry to a Regulatory Authority for the approval to market of a medicinal product for human use. The application in this context typically will 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. The RPS standard used for eCTD v4.0 provides the opportunity to refer across applications. However, it is not allowed to make use of this option for the initial submission unit applying for a marketing authorisation and eCTDv4.0 identifier cannot be used for previously submitted eCTD v 3.2.2 sequences as long as the transition messages has not been submitted. Submissions and submission units for regulatory activities after this initial one may refer to several applications at the same time.

An application will consist over time of multiple submissions or regulatory activities (e.g., initial marketing authorisation application, variations or PSURs). 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 6.1. controlled vocabulary

of submission types) will have its own regulatory action, and most likely will be composed of one or more submission units.

The ***application*** element is presented also 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.

9.15.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>component5>>application***

Refer to Table 3: XML Structure for the XML representation.

9.15.2 XML details

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

9.15.3 Terminology

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

9.15.4 Related Elements

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

- ***holder.applicant*** (see Section 9.12)
- ***informationRecipient.territorialAuthority*** (see Section 9.17)
- ***subject8.reviewProcedure*** (see Section 9.18)
- ***reference.applicationReference*** (see Section 9.19)

9.16 Applicant

The Applicant element is presenting the role of the sponsor of the initiation of a marketing authorisation application and is mentioned in relation to ***applicant*** element**.**

9.16.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>component5>>application>>holder>>applicant***

Refer to Table 3: XML Structure for the XML representation.

9.16.2 XML details

XML Elements

Note: The explanation will be provided in one of the future versions

*The **classCode** is fixed to "SPNSR". This value is not required in the XML message.*

XML Sample: Applicant

The following is an example of the XML for the applicant information. The applicant enters as a ***holder*** element between ***Submission*** and ***Application***.

```
<holder>
  <applicant>
    <sponsorOrganisation>
      <name xsi:type="BAG_EN">
        <item>
        <!--Code - 123456789 is the DUNS Number for the company Name-->
        <part value="Good Drugs" code="123456789" codeSystemVersion="OID for
DUNandBradstreet"/>
        </item>
      </name>
    </sponsorOrganisation>
  </applicant>
</holder>
...
```

See XML Color Legend for color usage

9.17 Territorial Authority (as information recipient related to application)

This element refers to the recipients receiving the submission unit / submission and being involved into the procedure. In consequence those recipients need to be named in whose country the medicinal product is applied for being marketed.

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

9.17.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>component5>>application>>informationRecipient>>territorialAuthority***

Refer to Table 3: XML Structure for the XML representation.

9.17.2 XML details

XML Elements

For the complete set of XML elements and attributes required for the ***territorialAuthority*** element see Section 9.4.

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

XML Sample: Territorial Authority

```
<informationRecipient>
 <territorialAuthority>
  <territory>
  <code code="FR" />
  </territory>
  <governingAuthority>
   id root="52345678-1234-1234-1234-12345678901" />
  <name>
  <part value="ANSM" code="FR-ANSM" />
  </name>
  </governingAuthority>
 </territorialAuthority>
</informationRecipient>
<informationRecipient>
 <territorialAuthority>
  <territory>
  <code code="NL" />
  </territory>
  <governingAuthority>
   id root="62345678-1234-1234-1234-12345678901" />
  <name>
  <part value=" MEB " code=" NL-MEB " />
  </name>
  </governingAuthority>
 </territorialAuthority>
</informationRecipient>
<informationRecipient>
 <territorialAuthority>
  <territory>
  <code code="DE" />
```

```
        </territory>
        <governingAuthority>
          id root="72345678-1234-1234-1234-12345678901" />
        <name>
        <part value=" BFARM " code=" DE-BFARM " />
        </name>
        </governingAuthority>
      </territorialAuthority>
    </informationRecipient>
```

9.17.3 Terminology

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

9.18 Review Procedure

The ***reviewProcedure*** defines the type of procedure to assess the marketing authorisation application whether it is a Centralised, decentralised, mutual recognition or purely national procedure

9.18.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>component5>>application>> subject8>>reviewProcedure***

Refer to Table 3: XML Structure for the XML representation.

9.18.2 XML details

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

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
	root	[1..1]	Valid OID or UUID	This is the root attribute that uniquely identifies the review procedure type
	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 ***id*** 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: • ***id@extension*** • ***id@identifierName*** • ***id@scope*** • ***id@reliability*** • ***id@displayable***			

XML Sample: ReviewProcedure

Note: Examples for XML snippets will be provided in one of the future versions

See XML Color Legend for color usage

9.18.3 Terminology

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

9.19 Application Reference

The ***applicationReference*** element is presenting the type of reference in specific application types, e.g. generic products. The element is not required in case a reference does not need to be provided. In case of an informed consent application or a generic product the reference product is mandated to be named.

9.19.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>component5>>application>>reference>>applicationReference***

Refer to Table 3: XML Structure for the XML representation.

9.19.2 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.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
	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 application number being referenced.
Conformance	The ***id*** is a required element required for the ***applicationReference*** element if to be submitted.			
Business Rules	This element must be used in case of generic products or the application is submitted by informed consent.			
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***			

947

948 ***ApplicationReference.reasoncode***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[1..1]		This code is related to the reason why reference can be made.
	code	[1..1]		

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	Only if reference is made the reason code is mandatory.			
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***code@codeSystemName*** • ***code@codeSystemVersion*** • ***code@valueSet*** • ***code@valueSetVersion*** • ***code@displayName*** • ***code@originalText*** • ***code@codingRationale*** • ***code@translation*** • ***code@source***			

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=" 5.993452.56789.12345" extension=" ema002156-001"/>
      <reasonCode>
        <!-- Reference medicinal product chosen for the demonstration of bioequivalence -->
        <item code="BE-Ref-Product" codeSystem="OID for EU Application Reference
Codes"/>
      </reasonCode>
    </applicationReference>
</reference>
```

See XML Color Legend for color usage

9.19.3 Terminology

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

9.20 Document

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

Document elements (e.g., PDF files) are prepared by the Applicant for review by the Regulatory Authority. In case of a Regulatory Authority that will send a submission unit to Applicants, the ***document*** elements are prepared by the Regulatory Authority. A ***document*** element will be submitted with a reference to one file and is referenced by one ***contextOfUse*** element. Documents can be grouped using a group title provided with the ***contextOfUse***. Documents can be referenced by multiple ***contextOfUse*** elements, and may be used in multiple submission units.[14]

Note to Implementers: For simple documents, the text element should be provided. For compound documents, the component element should be used instead to indicate the documents that make up the compound document.

9.20.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>component5>>application>>component6>>document***

Refer to Table 3: XML Structure for the XML representation.

[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 files and documents, those terms have been previously used interchangeably.

9.20.2 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.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				
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***id@extension*** • ***id@identifierName*** • ***id@scope*** • ***id@reliability*** • ***id@displayable***			

Document.title

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
title		[0..1]		This is a container element that provides the title for the document in the associated assignment
	extension	[0..1]		…….
Conformance	The ***title*** is an optional element			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Business Rules				
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***title@displayable***			

1002

1003

1004 ***Document.text***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
text		[0..1]		This is a container element that provides additional information about the document, including but not limited to: relative file path of the file in the submission contents, language, media type and integrity checksum information.…….
	integrityCheckAlgorithm	[1..1]	Alpha Numeric *e.g., SHA256*	This is the type of ***integrityCheckAlgorithm*** that was used for the checksum values provided in ***integrityCheck*** element.
	mediaType	[0..1]	Alpha Numeric *Refer to Section 4.*	This is the ***mediaType*** attribute that specifies the usage of the file where it is regionally requested.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
language		[0..1]		This is the container element that organises the coded value for the language.
	code	[1..1]	Alpha Numeric	The ***code*** attribute is a unique value that indicates the type of language controlled vocabulary (e.g., en, de, fr, etc.) see Section 6.3
	codeSystem	[1..1]	Valid OID	The ***codeSystem*** attribute is a unique identifier that indicates the controlled vocabulary system. *This should be the OID registered for the code system.*
text.reference		[0..1]		This is the container element within the ***text*** element for a document.
	value	[1..1]	Alpha Numeric File path of the document *e.g., "../m3/32-body-data/32s-drug-sub/32s1-gen-info.pdf"*	This is the ***value*** attribute of the ***text*** element that provides the location of the document with the relative path and filename of the document.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
text.integrityCheck		[1..1]	Alpha Numeric *e.g., "618102bf07065bcc1250594201fe448515f0fa61"*	This is the integrity check element, which has the checksum value.
Conformance	Documents require the following elements/attributes: • The ***text*** element o The ***text@IntegrityCheckAlgorithm*** attribute o The ***reference@value*** attribute o The ***text.integrityCheck*** element			
Business Rules	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. For file reuse, the ***text*** element must indicate the same ***reference@value***, ***text@IntegrityCheckAlgorithm*** and ***text.integrityCheck*** values of the previously submitted ***document*** element.			
Excluded Elements and Attributes	No other elements than indicated in the ICH eCTD v4.0 IG will be excluded.			

1005

1006

1007 ***Document.confidentialityCode***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[0..1]		This is a container element that provides …….
	root	[1..1]	Valid OID or UUID	This is the code attribute that …….

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
	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 ***cnfidentialityCode*** is an optional element			
Business Rules	If the element is provide a code and a root is required.			
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***			

XML Samples

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

```
<component>
  <document>
    <id root="0CE22887-210F-472C-B318-9E9FB7E7B0BC"/>
```

```
    <!--Code is only used for further identifying simple documents that are part of a compound
document and for which the controlled vocabulary has been defined-->
    <code code= “b12345”codeSystem=“8.13.850.1.223354.0.121.322”/>
    <title value=“General Information”/>
    <text integrityCheckAlgorithm=“SHA256” <text language=“en” />
      <text reference value=“../../ m1/eu/16-environrisk/161-nongmo/nongmo-
var.pdf”/>
      <integrityCheck>56df6492f724ee2e76e12cb4b001bd2fdc43603fb15
d70afc89813398739fb9c</integrityCheck>
    </text>
    <statusCode code=“active”/>
    <setIdroot=“12345678-4321-4321-4321-123456789987”/>
    <versionNumbervalue=“1”/ >
    ...
          [Additional information may appear after the addition of the text (if one exists, otherwise this will
          follow the component. For example, depending on the type of document the following elements
          may be available to select from the Document – component, sequelTo, referencedBy]
    ...
  </document>
</component>


<component>
  <document>
    <id root="9CF93E08-5C28-4D6D-B907-BFBE34F4119D" />
    <title value="Cover Letter for DE" />
    <text integrityCheckAlgorithm="SHA256" language="de">
    <reference value="../../m1/eu/10-cover/de/de-cover.pdf" />
    <integrityCheck>b9a6aff775736cf100505af68da859a941432a9f9e56d245ac3e
daa4235df0ac</integrityCheck>
    </text>
      <! ============================================== -->
      <!-- Commercial Confidential Informationand Protected Personal Data-PPD in EU: -->
      <!-- L =Low   -->
      <!-- M=Moderate   -->
      <!-- N=Normal   -->
      <!-- U=Unrestricted   -->
      <!-- R=Restricted   -->
      <!-- V=Very Restricted   -->
      <!-- ============================================== -->
    <confidentialityCode code="L"/>
  </document>
</component>
```

See XML Color Legend for color usage

Note to Implementers: For documents (i.e., representing each a single file), the text element will be provided along with the other required elements. Documents will have a keyword code to further specify the file tags for the document, e.g., smpc, according to the respective controlled vocabulary (see Section 6.1)

9.20.3 Terminology

The ***document*** element has one coded terminology for language (the ISO language codes) (see Section 6.3) . Regarding the document type code (see Section 6.1). in Module 1.3.1 only, ***document*** elements must provide this type of information by using the respective keyword definition.

9.21 Keyword Definition

The ***keywordDefinition*** element is used to define a keyword by the sender that is referenced by identifier in other parts of the message. For details see ICH Implementation guide. The usage of this element is expected to be helpful in EU Module 1 for product information text to separate different pharmaceutical forms or strengths and the document type.

9.22 Review

The ***review*** element is related to the regulatory activity (as defined by the submission), is associated with the holder and an author in the meaning of the Reference Member State or responsible authority, e.g. EMA in Centralised procedures, and refers to the product and the product category.

Optionally, additional information about the reference member state and the applicant can be provided, but will not be required for the EU.

9.22.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>subject4>>review***

Refer to Table 3: XML Structure for the XML representation.

9.22.2 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				
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***id@extension*** • ***id@identifierName*** • ***id@scope*** • ***id@reliability*** • ***id@displayable***			

Review.statusCode

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
status		[1..1]		This is a container element that provides …….
	root	[1..1]	Valid OID or UUID	This is the root attribute that …….
Conformance	The ***status*** is a required element			
Business Rules				
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***id@extension*** • ***id@displayable***			

XML Sample: Review

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

Note: Examples for XML snippets will be provided in one of the future versions

See XML Color Legend for color usage

9.22.3 Terminology

The ***review*** element requires codes for the ***statusCode*** element.

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

9.22.4 Related Elements

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

- ***subject2.productCategory*** (see Section 9.23)
- ***subject3.RegulatoryStatus***(see Section 9.24)
- ***subject1.manufacturedProduct*** (see Section 9.25)
- ***holder.applicant*** (see Section 9.26)
- ***author.territorialAuthority*** (see Section 9.27)

9.23 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.

9.23.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>subject4>>review>>subject2>>productCategory***

Refer to Table 3: XML Structure for the XML representation.

9.23.2 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.*

1126

1127 ***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]	Valid OID or UUID	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.*
Conformance	The ***code*** and ***codeSystem*** is a required element			
Business Rules				
Excluded Elements and Attributes	The following attributes are not required by eCTD 4.0: • ***code@codeSystemName*** • ***code@codeSystemVersion*** • ***code@valueSet*** • ***code@valueSetVersion*** • ***code@originalText*** • ***code@codingRationale*** • ***code@translation*** • ***code@source***			

1128

1129

1130 The following is an example of the XML for ***ProductCategory***.

1131 `<subject2>`

```
    <productCategory>
      <!-- Product Category: Medicinal product containing chemical substance -->
      <code code="chemical" codeSystem="ProductCategory Code system OID"/>
    </productCategory>
</subject2>
```

See XML Color Legend for color usage

9.23.3 Terminology

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

9.24 Regulatory Status

The ***regulatoryStatus*** element defines the outcome of regulatory action on a submission.

The ***RegulatoryStatus*** element is to assign the status of a regulatory activity applied for once the authority has decided to respond to the applicant. This element will be used by Competent Authorities only and supports therefore two-way communication.

9.24.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>subject4>>review>>subject3>> regulatoryStatus***

Refer to Table 3: XML Structure for the XML representation.

9.24.2 XML details

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

XML Elements

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

1159 ***RegulatoryStatus.code***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[1..1]		This is a container element that identifies the regulatory status of the submission
	code	[1..1]	Alpha Numeric e.g., "Approved", "Withdrawn",	This is the ***code*** attribute for the coded value of the regulatory status assigned by the responsible CA
	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*** is a required element			
Business Rules	This element should be used by the responsible competent authority only, e.g. EMA in case of Centralised procedures or the RMS in case of DCP or MRP.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
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***			

1160

1161 ***RegulatoryStatus.effectiveTime***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
effective time		[1..1]		This is a container element that provides the time stamp when a new regulatory status is assigned.
	timestamp	[1..1]	timestamp (GREG) *"200004010315 20.34+00" means April 1, 2000, 3:15 and 20.34 seconds expressed for UTC*	This value describes the precise time of assigning a regulatory status.
Conformance	The ***effective time*** is a required element			

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

XML Sample: regulatoryStatus

```
<subject3>
   <regulatoryStatus>
      <code code="100000072097">
        <displayName value="Application for Marketing Authorisation received."/>
      </code>
   </regulatoryStatus>
</subject3>
```

See XML Color Legend for color usage

9.24.3 Terminology

The ***regulatoryStatus*** element requires codes for the ***code*** element (see Section 6.1).

9.25 Manufactured Product

This element must be selected in case of an eCTD v4.0 message concerning the initial application for a human medicinal product. This determines the role of a product in the national context within a DCP or MRP. 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 replace the annex 5.15 to the application form of the current Module 1.2 in the EU.

9.25.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>subject4>>review>>subject1>>manufacturedProduct***

Refer to Table 3: XML Structure for the XML representation.

9.25.2 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
	extension	[0..1]	Alpha Numeric *e.g., Wonderpil 200 mg coded tablets*	The ***extension*** attribute of the ***id*** element provides a location to specify a region-specific name of the manufactured product.
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@exrension*** • ***id@identifierName*** • ***id@scope*** • ***id@reliability*** • ***id@displayable***			

XML Sample: manufacturedProduct

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

```
<subject1>
 <manufacturedProduct>
  <id/>
  <manufacturedProduct>
   <asNamedEntity>
    <assigningTerritory>
     <code code="NL" />
     <name>
      <!-- Product name type and value -->
      <part value="Wonder Drug" language="nl" />
     </name>
    </assigningTerritory>
   </asNamedEntity>
   <ingredient>
    <activeIngredientSubstance>
     <name>
      <!-- Substance name type and value -->
      <part code="IND01" codeSystem="Active ingredient code system OID"
value="Pioglitazone hydrochloride" />
      <part code="IND02" codeSystem="Active ingredient code system OID"
value=" Metformin hydrochloride" />
     </name>
    </activeIngredientSubstance>
   </ingredient>
  </manufacturedProduct>
 </manufacturedProduct>
</subject1>
```

9.25.3 Related Elements

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

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

The ***product*** element provides the information about the name of the product as used per territory and its ingredient(s) depending on how many pharmaceutical active ingredients contained. The following is an example for one relevant product name (case 1) and two diffeent product names per each country in use for the same manufactured product (case 2):

Case 1

```
<subject1>
  <manufacturedProduct>
    <manufacturedProduct>
      <name>
        <item>
          <part code="Product Name Type code" codeSystem="Product Name Type code system OID"
value="Product Name" language="en"/>
        </item>
      </name>
      <asNamedEntity>
        <name>
          <item>
            <part value="authority name"/>
          </item>
        </name>
        <assigningTerritory>
          <code code="country code"/>
        </assigningTerritory>
      </asNamedEntity>
      <ingredient>
        <activeIngredientSubstance>
          <name>
            <part code="Substance Name Type(INN, USAN, etc)" codeSystem="Substance Name Type
code system OID" value="Substance Name"/>
          </name>
        </activeIngredientSubstance>
      </ingredient>
    </manufacturedProduct>
  </manufacturedProduct>
 </subject1>
```

Case 2

To have multiple product names (e.g., Refludan and Refludin), the product.name.item.part can be repeated, and alternatively, <subject1> can be repeated as well.

(1) if you repeat the product.name.item.part;

```
 <subject1>
  <manufacturedProduct>
    <manufacturedProduct>
      <name>
        <item>
          <part code="Product Name Type code" codeSystem="Product Name Type code system OID"
value="Refludan" language="en"/>
          <part code="Product Name Type code" codeSystem="Product Name Type code system OID"
value="Refludin" language="es"/>
        </item>
      </name>…….
```

(2) if you repeat the <subject1>;

```
<subject1>
  <manufacturedProduct>
    <manufacturedProduct>
```

```
        <name>
          <item>
            <part code="Product Name Type code" codeSystem="Product Name Type code system OID"
value="Refludan" language="en"/>
          </item>
        </name>
        <asNamedEntity>
          <name>
            <item>
              <part value="authority name1"/>
            </item>
          </name>
          <assigningTerritory>
            <code code="country code"/>
          </assigningTerritory>
        </asNamedEntity>
        <ingredient>
          <activeIngredientSubstance>
            <name>
              <part code="Substance Name Type(INN, USAN, etc)" codeSystem="Substance Name Type
code system OID" value="Substance Name1"/>
            </name>
          </activeIngredientSubstance>
        </ingredient>
      </manufacturedProduct>
    </manufacturedProduct>
  </subject1>
  <subject1>
    <manufacturedProduct>
      <manufacturedProduct>
        <name>
          <item>
            <part code="Product Name Type code" codeSystem="Product Name Type code system OID"
value="Refludin" language="es"/>
          </item>
        </name>
        <asNamedEntity>
          <name>
            <item>
              <part value="authority name2"/>
            </item>
          </name>
          <assigningTerritory>
            <code code="country code"/>
          </assigningTerritory>
        </asNamedEntity>
        <ingredient>
          <activeIngredientSubstance>
            <name>
              <part code="Substance Name Type(INN, USAN, etc)" codeSystem="Substance Name Type
code system OID" value="Substance Name1"/>
            </name>
          </activeIngredientSubstance>
        </ingredient>
      </manufacturedProduct>
    </manufacturedProduct>
```

```
</subject1>
```

9.26 Holder

This element is referencing the details of the ***applicant*** element (see Section 9.16).

9.27 Territorial Authority (as author of review)

This element refers to the author of the review in the meaning of the Reference Member State or responsible authority, e.g. EMA in Centralised procedures, and refers to the product and the product category and states the respective authority and the territory of responsibility. This element will be used if the message is created by Regulatory Authority sending back e.g. the Assessment Report or List of Questions.

9.27.1 Location in XML

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

- ***controlActProcess>> subject>> submissionUnit>>component1>> submission>>subject4>>review>>subject1>>author>>territorialAuthority***

Refer to Table 3: XML Structure for the XML representation.

9.27.2 XML details

XML Elements

For the complete set of XML elements and attributes required for the ***territorialAuthority*** element see Section 9.4.

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

XML Sample: author.territorialAuthority

```
<subject2>
  <review>
    <id></id>
    <statusCode><statusCode />
    <author>
    <territorialAuthority>
      <name>
      <!—Assessment authoring authority -->
      <part code="ansm" value=" L'Agence nationale de sécurité du médica
      ment et des produits de santé " codeSystem="Authority Code syst OID" />
      </name>
    </territorialAuthority>
```

```
        </author>
      </review>
    </subject2>
```

9.28 Category Event

The ***categoryEvent*** element will not be used in the EU.

This class will currently not be used in EU Module 1 part of an eCTD v4.0 message, because documentation submitted in eCTD format will not be required for event types such as scientific advice or regulatory advice.

10. 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 and to 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, e.g. grouped variation, workshare procedures and submissions in Decentralised and Mutual Recognition Procedures.

10.1 Individual Components

10.1.1 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 in MRP/DCP:

```
<subject1>
  <!-- to have multiple product name (e.g. WonderMat in Germany, Wonder Drug in NL,
WonderPil in UK and PileWonder in France -->
  <manufacturedProduct>
    <id />
    <manufacturedProduct>
      <name>
        <item>
          <part value="WonderMat" language="de"/>
        </item>
      </name>
      <asNamedEntity>
        <name>
          <item>
            <part value="BfArM" language="de"/>
          </item>
        </name>
        <assigningTerritory>
          <code code="DE"/>
        </assigningTerritory>
      </asNamedEntity>
      <ingredient>
        <activeIngredientSubstance>
          <name>
```

```
1438            <part code="IND01" codeSystem="Substance Name Type code system OID"
1439    value="Pioglitazone hydrochloride"/>
1440            <part code="IND02" codeSystem="Substance Name Type code system OID"
1441    value="Metformin hydrochloride"/>
1442          </name>
1443        </activeIngredientSubstance>
1444      </ingredient>
1445    </manufacturedProduct>
1446  </manufacturedProduct>
1447 </subject1>
1448 <subject1>
1449   <manufacturedProduct>
1450    <id />
1451    <manufacturedProduct>
1452      <name>
1453        <item>
1454          <part code="Wonder drug" language="NL"/>
1455        </item>
1456      </name>
1457      <asNamedEntity>
1458        <name>
1459          <item>
1460            <part value="MEB"/>
1461          </item>
1462        </name>
1463        <assigningTerritory>
1464          <code code="NL"/>
1465        </assigningTerritory>
1466      </asNamedEntity>
1467      <ingredient>
1468        <activeIngredientSubstance>
1469          <name>
1470            <part code="IND01" codeSystem="Substance Name Type code system OID"
1471    value="Pioglitazone hydrochloride"/>
1472            <part code="IND02" codeSystem="Substance Name Type code system OID"
1473    value="Metformin hydrochloride"/>
1474          </name>
1475        </activeIngredientSubstance>
1476      </ingredient>
1477    </manufacturedProduct>
1478  </manufacturedProduct>
1479 </subject1>
1480 <subject1>
1481   <manufacturedProduct>
1482    <id />
1483    <manufacturedProduct>
1484      <name>
1485        <item>
1486          <part code="Wonder Pil" language="EN"/>
1487        </item>
1488      </name>
1489      <asNamedEntity>
1490        <name>
1491          <item>
1492            <part value="MHRA"/>
```

```
            </item>
          </name>
           <assigningTerritory>
             <code code="UK"/>
           </assigningTerritory>
        </asNamedEntity>
        <ingredient>
          <activeIngredientSubstance>
            <name>
              <part code="IND01" codeSystem="Substance Name Type code system OID"
value="Pioglitazone hydrochloride"/>
              <part code="IND02" codeSystem="Substance Name Type code system OID"
value="Metformin hydrochloride"/>
            </name>
          </activeIngredientSubstance>
        </ingredient>
      </manufacturedProduct>
    </manufacturedProduct>
  </subject1>
  <subject1>
    <manufacturedProduct>
      <id />
      <manufacturedProduct>
        <name>
          <item>
            <part code="Pile Wonder" language="EN"/>
          </item>
        </name>
        <asNamedEntity>
          <name>
            <item>
              <part value="ANSM"/>
            </item>
          </name>
           <assigningTerritory>
             <code code="FR"/>
           </assigningTerritory>
        </asNamedEntity>
        <ingredient>
          <activeIngredientSubstance>
            <name>
              <part code="IND01" codeSystem="Substance Name Type code system OID"
value="Pioglitazone hydrochloride"/>
              <part code="IND02" codeSystem="Substance Name Type code system OID"
value="Metformin hydrochloride"/>
            </name>
          </activeIngredientSubstance>
        </ingredient>
      </manufacturedProduct>
    </manufacturedProduct>
  </subject1>
```

10.1.2 Managing Country Specific Processing Numbers

Only in 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="fr-2083-001-dc" extension="de-2189072"/>
            <item root="fr-2083-001-dc" extension="nl-456789"/>
            <item root="fr-2083-001-dc" extension="uk-341974"/>
            <item root="fr-2083-001-dc" 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>
```

10.1.3 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 from the product structure – information regarding pharmaceutical form or strength this text is dedicated to be used. These metadata will be assigned using different elements of the eCTD XML message:

The ***document.text*** element holds a ***language*** element

The ***document*** element holds a ***code*** element specifying document types like “smpc” or” pl”.

A keyword from the controlled vocabulary of ISO country codes specifies the country of applicability.

A keyword value from the sponsor defined ***keywordDefinition*** of pharmaceutical form or strength will allow a presentation of the set of product information texts provided in the QRD template per pharmaceutical form or strength.

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

XML example:

```
-<component>
    <priorityNumber value="1"/>
    -<contextOfUse> <id root="12345678-1234-5678-3456-127536489712"/>
```

```
<!-- CTD Heading -->
-<code codeSystem="Code system OID " code="m131-smpclabelpl">
    <displayName 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 (if needed to be specified) -->
    -<territorialAuthority>
        -<territory>
            <code codeSystem="FR" codeSystemName="country code system name"/>
        </territory>
    </territorialAuthority>
</primaryInformationRecipient>
-<derivedFrom>
    -<documentReference>
        <id root="12345678-1234-1234-1234-198765432198" extension="12345"/>
    </documentReference>
</derivedFrom>
-<subjectOf negationInd="1"/>
    <!-- The SubmissionReference element is used to indicate when a ContextOfUse is not
        relevant to a specific Submission within a submissionUnit.-->
    -<submissionReference>
        <id>
            <item root="12345678-1234-5678-3456-127536489712"/>
        </id>
    </submissionReference>
    <referencedBy typeCode="REFR">
        <keyword>
            <code codeSystem="SmPC Label PL" codeSystemName="cdocument type code
system name"/>
        </keyword>
    </referencedBy>
</subjectOf>
</contextOfUse>
</component>
```

10.2 Content Management (contextOfUse and Documents)

There are no deviating principles to apply in case of 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 addition of the **Application.code**, for example any of the following elements related to **holder, informationRecipient, ReviewProcedure, Application.Reference**]*

```
<component>
    <document>
        <id root="12345678-5555-5555-5555-555555550001"/>
        <title value="Cover Letter"/>
        <text integrityCheckAlgorithm="SHA256">
        <reference value="../../m1/eu/10-cover/common-cover-20120420.pdf"/>
        <integrityCheck>3285a776897425b9a3b87abbaaf163fb261242397997b003efe3201e</integrityCheck>
        </text>
        <statusCode code="active"/>
        <setId root="57694301"/>
        <versionNumber value="1"/>
    </document>
</component>
<component>
    <document>
        <id root="12345678-5555-5555-5555-555555550001"/>
        <title value="Tracking Table"/>
        <text integrityCheckAlgorithm="SHA256">
        <reference value="../../m1/eu/10-cover/common-cover-tracking-20120420.pdf"/>
        <integrityCheck>3285a776xv745a25b9a3b87abbaaf163f726ec91242397997b003efe3201e</integrityCheck>
        </text>
        <statusCode code="active"/>
        <setId root="573421301"/>
        <versionNumber value="1"/>
    </document>
</component>
<component>
    <document>
        <id root="12345678-5555-5555-5555-555555550002"/>
        <title value="Expert Quality"/>
        <text integrityCheckAlgorithm="SHA256">
        <reference value="../../m1/eu/14-expert/141-quality/quality-meier.pdf"/>
        <integrityCheck>3285a776897425b9a3b877z45abbaaf1726ec91242397997b003efe3202e</integrityCheck>
        </text>
        <statusCode code="active"/>
        <setId root="29872638"/>
        <versionNumber value="1"/>
    </document>
</component>
<component>
    <document>
        <id root="12345678-5555-5555-5555-555555550003"/>
        <title value="Expert Non-Clinical"/>
        <text integrityCheckAlgorithm="SHA256">
        <reference value="../../m1/eu/14-expert/142-nonclinical/nonclinical-schulz.pdf"/>
        <integrityCheck>3285a776897425b9a3b87abbaaf16
            3fb2646726ec91242397997b003efe3203e</integrityCheck>
        </text>
        <statusCode code="active"/>
        <setId root="6910897729"/>
        <versionNumber value="1"/>
```

```
            </document>
        </component>
    </application>
</componentOf>
```

The respective folder structure is provided below:

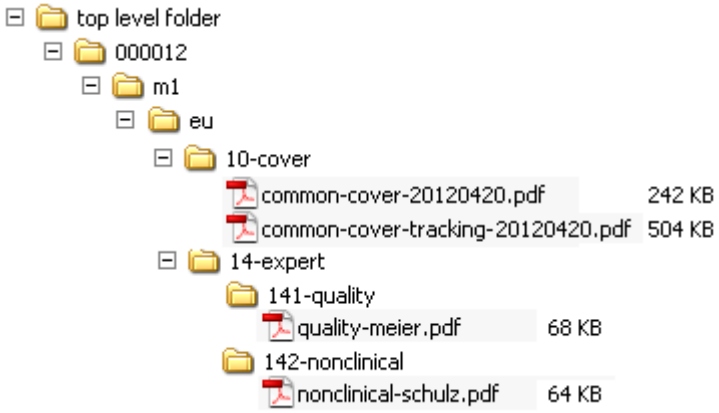


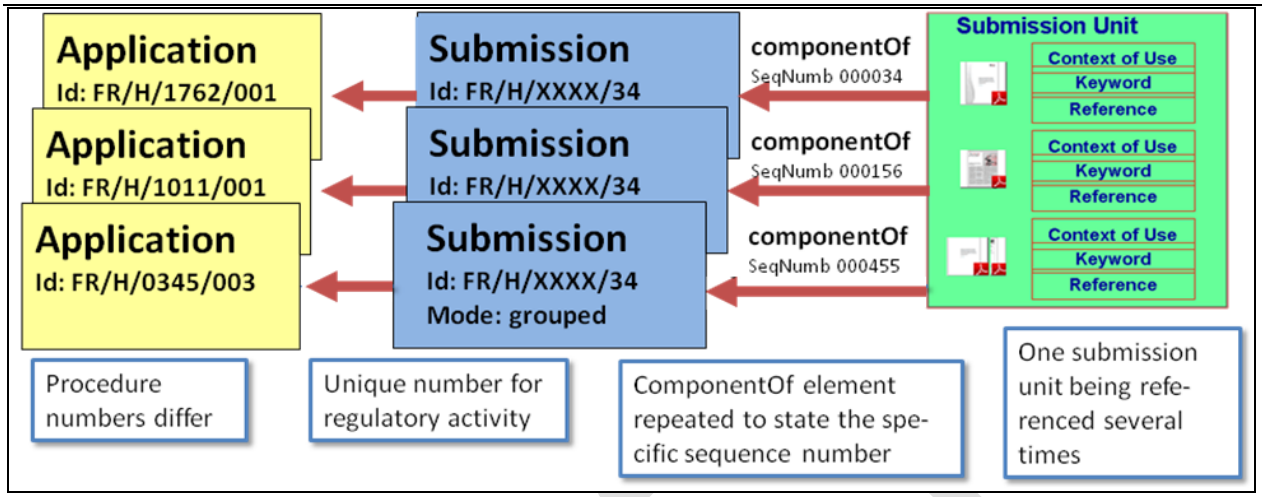
Figure 2: Folder structure related to submission unit message

10.3 Complex Scenarios

10.3.1 Referencing Multiple Applications in Case of Grouping or Worksharing Regulatory Activities (Submissions)

Grouped and workshared variations are the only business cases for sending a Submission Unit with more than one ***componentOf.Submission*** element (e.g., manufacturing changes that affect more than one application) to associate this ***submissionUnit*** via multiple ***submission*** elements to all ***applications*** concerned by the grouped variation or workshared procedure.

Figure 3: Referencing multiple applications



Top level folder will be fr034g.

The second level folder 999900 contains sequence number 34 of application FR/H/1762/001 and below that all relevant documents according to structure outline in Annex 1 and ICH eCTD IG.

For sequence number 156 of application FR/H/1011/001 and sequence number 455 of application number FR/0345/001 is is not needed to submit files physically. They will be referenced by the submission unit xml file and can be displayed as being submitted physically.

In case of a different grouping the top level folder may be named ’fr072g’ or in case of a worksharing ‘de045ws’.

The second level folder 999900 concerning sequence number 000172 of application 1762.

XML example:

```
<subject typeCode="SUBJ">
    <submissionUnit>
        <id></id>
        <code></code>
        <title></title>
        <statusCode></statusCode>
        <callBackContact>
            <contactParty>
                ...
            </contactParty>
        </callBackContact>
        <component>
            <priorityNumber value="1"/>
            <contextOfUse>
                ...
            </contextOfUse>
        </component>
        <componentOf>
            <sequenceNumber>
    <sequenceNumber value="34"/>
```

```
                </sequenceNumber>
                <submission>
                    <id/>
                    <item root="Globally unique submission ID" extension="FR/H/XXXX/34" />
                    <code code="var-type2" codeSystem="Submission Type Code system OID" codeSystemName="Submission
Type Codes " />
                    <subject1>
                        <mode>
                            <id/>
                            < code="grouped" />
                        </mode>
                    </subject1>
                    <subject2>
                        <review>
                        - <author>
                                ....
                        </author>
                        </review>
                    </subject2>
                ° </submission>
            </component>
            -<componentOf>
                -<application>
                    <id xsi:type="DSET_II">
                        <item root="fr-1762-001-dc"
                    </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>
            °</component>
            -<component>
                <sequenceNumber>
<sequenceNumber value="156"/>
                </sequenceNumber>
                <submission>
                    <id/>
                    <item root="Globally unique submission ID" extension="FR/H/XXXX/34" />
                    <code code="var-type2" codeSystem="Submission Type Code system OID" codeSystemName="Submission
Type Codes " />
                    <subject1>
                        <mode>
                            <id/>
                            < code="grouped" />
                        </mode>
                    </subject1>
                    <subject2>
                        <review>
                        - <author>
                                ....
                        </author>
                        </review>
                    </subject2>
                ° </submission>
            </component>
            -<componentOf>
                -<application>
                    <id xsi:type="DSET_II">
                        <item root="fr-1011-001-dc"
                    </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>
            -</component>
            -<component>
```

```
                    <sequenceNumber>
      <sequenceNumber value="455"/>
                    </sequenceNumber>
                    <submission>
                     ....
                    ° </submission>
                  </component>
                 -<componentOf>
                      -<application>
                           ....
                       </application>
                  </componentOf>
            </submission>
  </componentOf>
  </submissionUnit>
  </subject>
```

The complete section needs to be repeated as needed by number of applications involved.

10.3.2 Update of Product Information Texts (SmPC, PL) in Response to Regulators Assessment of a Grouped Variation

Due to a PRAC recommendation a Type II variation to update the wording of the SmPC and PL for a number of products across a range of MAs is submitted as a Grouped Variation. France is the RMS with the UK, Ireland and Netherlands as CMS. The previously submitted documents need to be updated.

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	0019	Pile Wonder 10mg tablets - FR Wonder Pills 10mg tablets - UK &IR Wonder Drug 10mg tablets - NL
id: FR/H/xxxx/II/003G	FR/H/1762/002/II/002/G	0019	Pile Wonder 20mg tablets -FR Wonder Pills 20mg tablets - UK &IR Wonder Drug 20mg tablets - NL
id: FR/H/xxxx/II/003G	FR/H/1011/001/II/003/G	0054	Pile Wonder 10mg capsules -FR Wonder Pill 10mg capsules - UK& IR Wonder Drug 10mg capsules - NL
id: FR/H/xxxx/II/003G	FR/H/0345/001/II/003/G	0024	Pile Wonder 10mg/ml Solution for Infusion -FR Wonder Pill 10mg/ml Solution for Infusion - UK & 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" xsi:schemaLocation="urn:hl7-org:v3
RPS_FlatSchema_Jan2012Ballot.xsd" xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-
instance">
<subject typeCode="SUBJ">
  <submissionUnit>
    <id>=“78965412-3214-5698-7856-985412563254”/</id>
    <code> code=“response to questions” codeSystem=“Submission Unit  code system OID”/</code>
    <title>Response to Questions</title>
    <statusCode> code=“active”</statusCode>
    <component>
      <priorityNumber value="1" />
        <contextOfUse>
          <id root="12345678-1234-5678-3456-127536489712" />
        <code code=" m1-3-1-spc-label-pl " codeSystem="EU M1 CoU Code system OID for SmPC">
        <displayName value="1.3.1 SmPC" />
        <statusCode code="active" />
        <primaryInformationRecipient>
          <territorialAuthority>
            <territory>
              <code code="FR" codeSystem="country code system OID"
              codeSystemName="country code system name" />
            </territory>
            <governingAuthority>
              <id root="52345678-1234-1234-1234-12345678901" />
              <name>
                <part value="ANSM" code="FR-ANSM" />
              </name>
            </governingAuthority>
          </territorialAuthority>
        </primaryInformationRecipient>
        <replacementOf="RPLC">
          <relatedContextOfUse>
            <id root="87454521-9874-6541-1236-159842345687" />
            <versionNumber value="1" />
          </relatedContextOfUse>
        </replacementOf>
        <derivedFrom>
          <documentReference>
            <id root="12345678-1234-1234-1234-198765432198" extension="12345" />
          </documentReference>
        </derivedFrom>
        <subject7 />
          <submissionReference>
            <id xsi:type="DSET_II">
              <item root="12345678-1234-5678-3456-127536489712" />
             </id>
          </submissionReference>
```

This section need to be repeaed as often as CoU need to be included, e. g. for cover letter, tracking table, variation form

This section will point to the previous version of the SmPC and will be repeated as many as documents will be replaced.

```
        </subject7>
        <referencedBy typeCode="REFR">
          <keyword>
            <code code=" m1-3-1-spc-label-pl " codeSystem="EU M1 CoU system OID"
            codeSystemName="EU M1 CoU Codes " />
          </keyword>
        </referencedBy>
        </contextOfUse>
      </component>
      <componentOf1 >
        <sequenceNumber>
          <sequenceNumber value="000019"/>
        <submission>
          <id></id>
            <item root="Globally unique submission ID" extension="FR/H/XXXX/34" />
            <code code="var-type2" codeSystem="Submission Type Code system OID"
            codeSystemName="Submission Type Codes " />
        </submission>
        <callBackContact>
          <contactParty>
            ...
          </contactParty>
        </callBackContact>
        <subject2>
          <review>
            <subject1>
              <regulatoryStatus>
                <code></code>
              </regulatoryStatus>
            </subject1>
          </review>
        </subject2>
        <subject5>
          <mode>
            <code="grouped" />
          </mode>
        </subject5>
         <componentOf>
          <application>
            <id xsi:type="DSET_II">
              <item root="fr-1762-001-dc" extension="fr-2189072"/>
              <item root="fr-1762-001-dc" extension="uk-pl/2012/13"/>
              <item root="fr-1762-001-dc" extension="ie-4523.23.1978"/>
              <item root="fr-1762-001-dc" extension="nl-mb-23419"/>
            </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]
                    ...
            <informationRecipient>
              <territorialAuthority>
                <governingAuthority>
```

The sequence number and following attributes including information recipient and application attribute need to be repeated as many as different sequences will be provided. In this example the grouping is related to three applications requiring three different sequence numbers..

This section need to be repeated as often as member states are involved in the procedure

```
            <id root="52345678-7890-1234-1234-12345678902" />
            <name>
              <part value="MHRA" code="UK-MHRA" />
            </name>
          </governingAuthority>
        </territorialAuthority>
      </informationRecipient>
      <subject8>
        <reviewProcedure>
          <code>mutual recognition</code>
        </reviewProcedure>
      </subjec8t>
    </application>
  </componentOf>
  <component>
    <document>
      <id>
        <id root="12345678-1234-1234-1234-198765432198" extension="12345" />
      </id>
      <title>Pile Wonder 10mg tablets </title>
      <text integrityCheckAlgorithm="SHA256"
          language="en">
          <reference value="../../m1/eu/131=SmPC/common=SmPC.pdf" xsi:type="TEL"/>"/>
        <integrityCheck>3285a776897425b9a3b87abbaaf163fb261242397997b003efe3201e</integrityCheck>
      </text>
      <referencedBy>
        <keywordDefinition>
          <code>100000155532</code>
          <statusCode>"active" </statusCode>
          <value>
            <item>
              <displayName>SmPC</displayName>
            </item>
          </value>
        </keywordDefinition>
      </referencedBy>
    </document>
  </component>
  <referencedBy>
    <keywordDefinition>
      <code></code>
        <statusCode></statusCode>
          <value >
            <item>
              <displayName></displayName>
            </item>
          </value>
        </keywordDefinition>
```

This section need to be repeaedt as often as documents need to be included, e. g. for cover letter, tracking table, variation form and PL

In case of additional keywords this section can be repeated.

```
        </referencedBy>    …
    </component>
                [A similar entry would be made for the application form]
                …
```

10.3.3 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 MAA as a group (see Section 9.13)

10.3.4 Referencing across submissions and applications of the same pharmaceutical company

The principles of referencing is entirely the same regardless whether a reference should be presented within a submission unit, where a document is to be displayed with two different context of use, or across submissions, or across applications. Always a ***document*** element will be referenced by the new ***contextOfUse*** element by its ID. The ***document*** element provides the link to the PDF-file. The ***document*** element ID needs to be known which might not work, if the compiling systems of different companies are not interoperable once the medicinal product was transferred to another MAH. In those cases a separate transition sequence is required to allow a mapping between the previous and the new document ID via a replacing ***contextOfUse*** element. As a general rule, no ***document*** elements can be referenced if they are not submitted to all member states involved. From technical point of view the rules outlined in the ICH eCTD IG apply entirely to EU Module 1 as well.

Remark: 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 when a document title change is allowed or recommended will be provided separately.

10.4 eCTD XML message from regulators

As it was the purpose of eCTD improvement version 4.0 to support two way communications, XML messages have to be built by regulators as well. These messages should include any type of assessment reports and list of questions, but in case of messages at the end of a procedure it should provide the updated regulatory statusas well, the authorisation letter and the finally agreed product information texts. Several elements relevant for a messages sent by applicants will not be needed by regulators. The following tables will illustrate the constrained part.

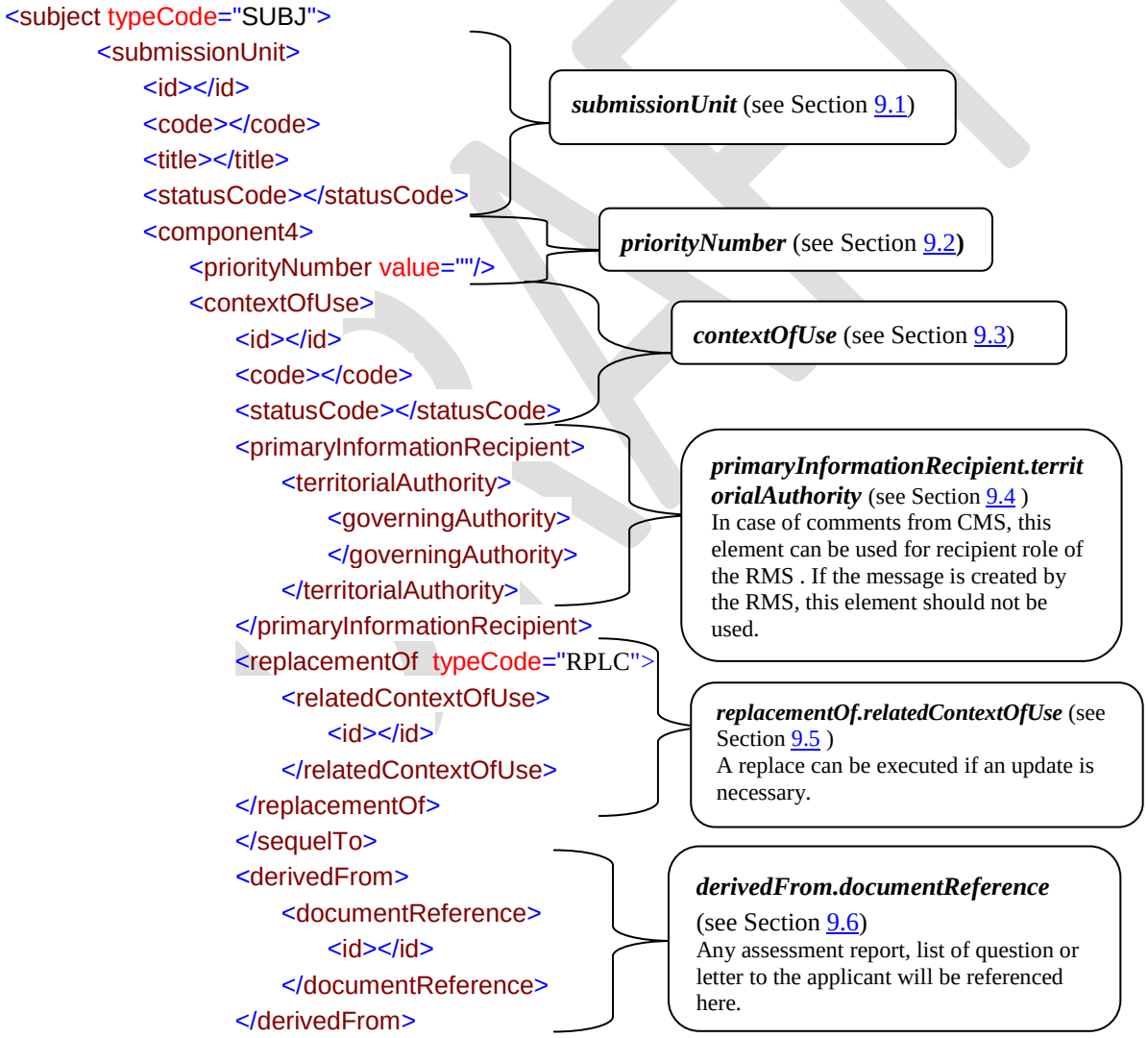
2031 **Table 4: XML Structure- Submission Unit from Regulators**

XML Structure

The eCTD begins by identifying the ***subject*** element of the XML message. The payload message starts with the ***submissionUnit*** element and relates the rest of the elements to the Submission Unit being sent. The ***submissionUnit*** element in case of a message from regulators contains the following elements and their attributes:

- ***component4.contextOfUse***
  - ***prioritNumber***
  - ***replacementOf.relatedContextOfUse***
  - ***derivedFrom.documentReference***
  - ***subject5.submissionReference***
  - ***referencedBy.keyword***
  - ***primaryInformationRecipient.TerritorialAuthority***
- ***component1.submisison***priorityNumber

Mandatory elements in the message



XML Structure

```
<subject5 negationInd="">
    <submissionReference>
        <id xsi:type="DSET_II">
            <item></item>
        </id>
    </submissionReference>
</subject5>
<reference1 typeCode="REFR">
    <keyword>
        <code></code>
    </keyword>
</reference1>
</contextOfUse>
</component4>
```

submissionReference
see Section 9.7)

Keyword (see Section 9.8)
as a supplement to the ICH Implementation Guide and specific for EU Module 1 Implementation Guide

2032

Table 5: XML Structure – Submission from Regulators

XML Structure

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

- ***sequenceNumber***
- ***callBackContact.contactParty***
- ***subject4.review***
- ***subject6.regulatoryReviewTime***
- ***subject7.submissionGroup***
- ***subject9.mode***

Mandatory elements in the message

```
<componentOf>
  <sequenceNumber></sequenceNumber>
    <submission>
      <id></id>
      <code></code>
      <callBackContact>
        <contactParty>
          <id></id>
          <statusCode></statusCode>
            <contactPerson>
            <name xsi:type="BAG_EN">
              <item><part/></item>
            </name>
            <telecom xsi:type="BAG_TEL">
              <item></item>
            </telecom>
          </contactPerson>
        </contactParty>
      </callBackContact>
      <subject4>
        <review>
        </review>
      </subject4>
        <subject3>
          <regulatoryStatus>
            <code></code>
          </regulatoryStatus>
        </subject3>
        <subject7>
          <submissionGroup>
            <id></id>
          </submissionGroup>
        </subject7>
```

sequenceNumber.submission
(see Section 9.9)
The same number as used by the applicant can be used extended by an indicator that this is a submission from a regulator, "r". The reviewing system need to use the time stamp of the header for display purpose.

submission (see Section 9.10)

callBackContact
(see Section 9.11)
Details of process management contact

review (see Section 9.22)
This will include information about the author (RMS) of e.g the assessment report.

regulatoryStatus (see Section 9.24)

submissionGroup (see Section 9.13)
This element is mandatoryonly if the assessment reports apply to more than one application.

2036 **Table 6: XML Structure - Application from Regulators**

XML Structure

This section of the XML relates to the ***application*** element. The application section contains the following elements and their attributes in case of a message from regulators:

- ***holder.applicant***
- ***informationRecipient.territorialAuthority***
- ***subject8.reviewProcedure***
- ***reference.applicationReference***
- ***component6.document***
  - ***referencedBy.keyword***
- ***referencedBy.keywordDefinition***

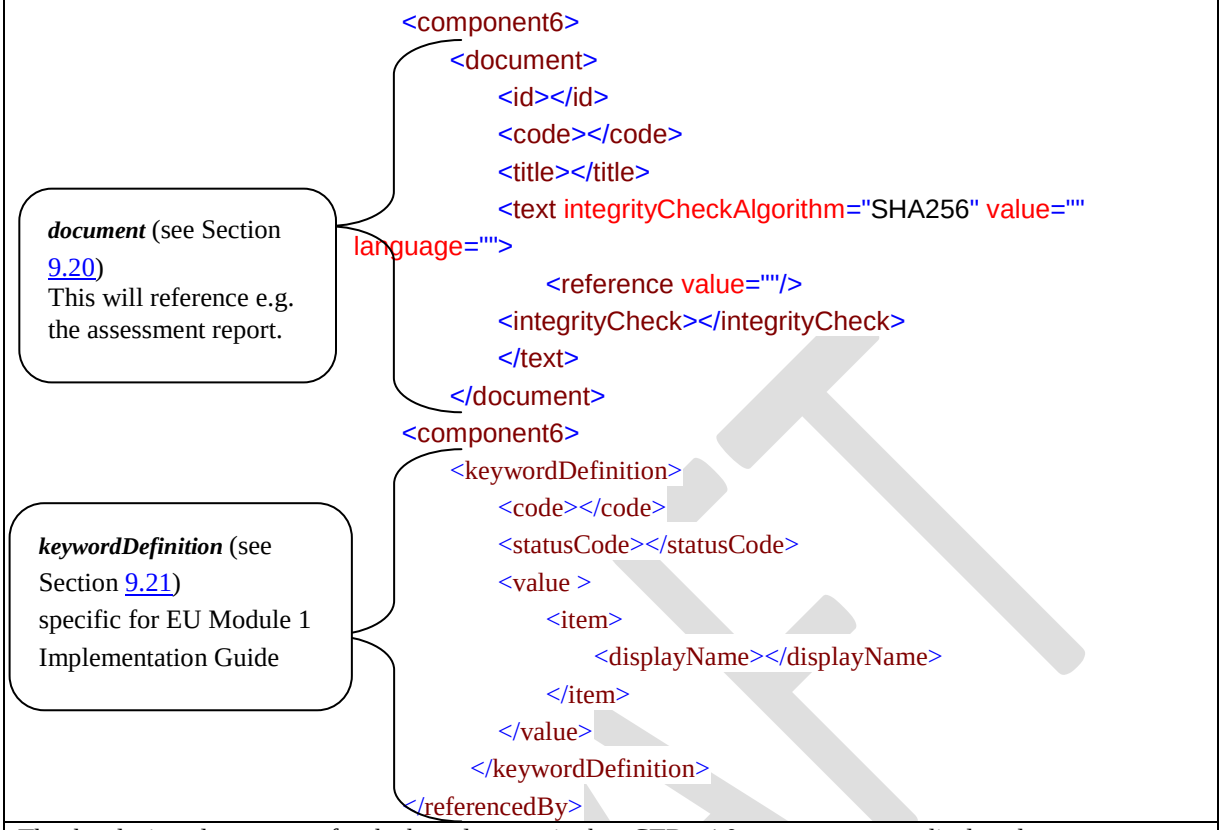
Mandatory elements in the message

```
<componentOf>
    <application>
        <id>
            <item root="" extension=""/>
        </id>
        <code></code>
        <informationRecipient>
            <territorialAuthority>
                <governingAuthority>
                    <id></id>
                    <name>
                        <part value=""/>
                    </name>
                </governingAuthority>
            </territorialAuthority>
        </informationRecipient>
```

application (see Section 9.15)

informationRecipient.territorialAuthority (see Section 9.17)
Details of the receiving member states)

XML Structure



The the closing element tags for the key elements in the eCTD v4.0 message are not displayed..

The most consistant way to make use of a sequence number will be to re-use the same as the sponsor's submission unit to which the regulators message responds extended by an indicator that this is a submission from a regulator, "r". It may be more appropriate to use some header information to allow differentiation between different regulating agencies sending their messages. A respective feature should be developed. The reviewing system needs to use the time stamp of the header for display purposes and to support an appropriate ordering: the incoming message can be presented first (receiving date at agency) and the outgoing message second (sending date by agency).

10.5 Building Regulatory Activities (Submission)

The following section provides a set of message snippets that highlight the Module 1 content. These XML samples do not include the information that is relevant to Modules 2-5. All samples in this section provide a regulatory activity life cycle within an application.

10.5.1 Marketing Authorisation Application (MAA)

Examples are provided in Appendix 2

10.5.2 Variation

Examples are provided in Appendix 2

11. XML MESSAGE VALIDATION RULES

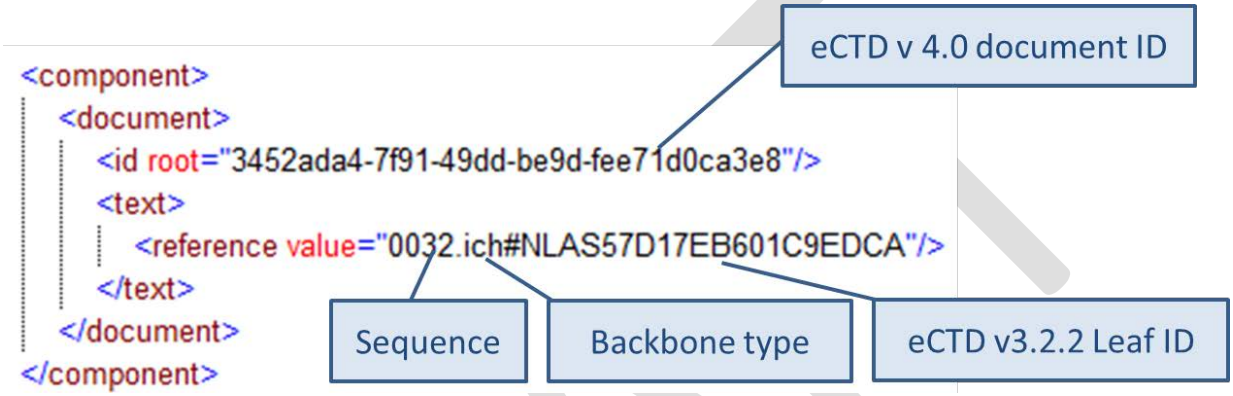
The principles of validation rules for eCTD v4.0 messages will not differ between regions. For details please refer to the ICH Implementation Guide. The following table highlights validation rules by elements which are specifally used in the EUAll checks according to the schema will not repeated here. All code values are expected to be currently valid.

Category	Type/Element	Validation Criteria
Message Validation	**Territorial Authority**	The Authority attribute must have a valid code value.
	Submission Reference	A submission unit sent by regulators must provide a Submission Reference stated as a valid code value
	Submission	Submission must have a valid code value
	Submission Group	Submission Group must have a valid code value.
		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 value
	Applicant	Applicant must have a valid code value
		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 starts with 1
	Application Reference	Applicantion Reference identifier is required (1..1)
		Application Reference must have a valid code value
	Review	Only one Review element can exist for a message.
		Review code must have a valid OID for the Code System value
		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 value

Category	Type/Element	Validation Criteria
	Regulatory Status	Only one Regulatory Status element can exist for a message
		Regulatory Status code must have a valid OID for the Code System value .

12. COMPATIBILITY AND REFERENCE TO EU MODULE 1 ECTD V2.0

The principles of forward compatibility will not differ between regions.



In case of the regional module the backbone type will be changed into ‘eu’ for the Module 1 of the EU region.

The ICH Implementation Guide describes a onetime transition from v3.2.2 to v4.0 based on the current regulatory view of a dossier. This means that all valid content of a dossier in eCTD format v3.2.2 will be mapped in a way that document elements can be referenced in the future according to the eCTD specification v4.0. This transition will work once the dossier volume is already re-baselined in eCTD v3.2.2. It needs to be carefully considered whether all parts of the dossier need to be included into a baseline. It needs to be noted that those parts which are not yet in eCTD format cannot be transitioned. According to current guidance baselines must not include large-volume modules like module 4 and 5.

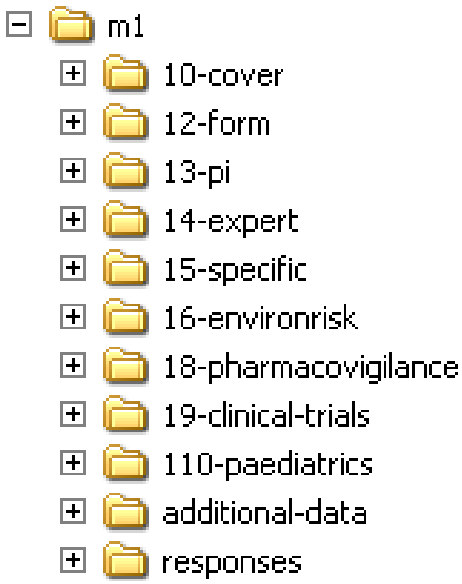
The transition workload will definitely depend from a business decision on whether a dossier need to be switched entirely to eCTD v3.2.2 in advance or whether it remains acceptable that only parts of a dossier are switched, or that the use of eCTD can start even with single documents. Transition to eCTD v4.0 will be possible only for those parts already in eCTD format v3.2.2. Any advantage of version 4.0 can be achieved only after transition.

Different from transition – forward compatibility from version 3.2.2 towards version 4.0 of eCTD submissions – guidance need to be established how current dossiers 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 SAMPLE FILES AND FOLDERS FOR EU MODULE 1 LITE FOLDER STRUCTURE

Module 1

Current Module 1 Folder Structure



Proposed Lite Module 1 Folder Structure

Note: Filenames provide sufficient specificity

APPENDIX 2 SAMPLE ECTD MESSAGES

This section includes general examples on marketing authorisation application and variation type 2 for illustration.

Marketing Authorisation application

```
<?xml version="1.0" encoding="UTF-8"?>
<PORP_IN000001UV xsi:schemaLocation="urn:hl7-org:v3 ../multicacheschemas/PORP_IN000001UV.xsd"
ITSVersion="XML_1.0" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance" xmlns="urn:hl7-
org:v3">
<id/>
<creationTime/>
<interactionId/>
<processingCode/>
<processingModeCode/>
<acceptAckCode/>
<receiver typeCode="RCV">
  <device determinerCode="INSTANCE" classCode="DEV">
    <id/>
  </device>
</receiver>
<sender typeCode="SND">
  <device determinerCode="INSTANCE" classCode="DEV">
    <id/>
  </device>
</sender>
<controlActProcess classCode="ACTN" moodCode="EVN">
  <subject typeCode="SUBJ">
    <submissionUnit>
    <!-- ================================================================== -->
    <!-- This is the root attribute that uniquely identifies the submission -->
    <!-- Create a new Decentralised Procedure application and submission -->
    <!-- Acme Pharmaceuticals has prepared information relating to its new product - Global Fixit -->
    <!-- The submission unit contains documentation that are common to all countries but also documentation -->
    <!-- that are specific to individual countries and languages -->
<!-- ================================================================== -->
      <id root="11953B86-AF49-408B-820D-67CF80D41C6A"/>
    <!-- ================================================================== -->
    <!-- Submission Unit Type = Initial submission to start a regulatory activity" -->
    <!-- ================================================================== -->
    <!-- EUTCT = "100000155047" short name ="initial" -->
    <!-- ================================================================== -->
      <code codeSystem="3.16.750.1.223354.0.121.521" code="100000155047"/>
      <title value="EU-300 test case – Sequence 1"/>
```

```
        <statusCode code="active"/>
    <!-- ========================================================================== -->
    <!-- the Reference Member State : RMS -->
    <!-- ========================================================================== -->
        <component>
          <contextOfUse>
            <id root="30A7CF17-5204-4C08-A936-JEE8746BE100"/>
            <statusCode code="active"/>
            <primaryInformationRecipient>
        <!-- RMS -->
              <territorialAuthority>
                <territory>
                  <code code="FR"/>
                </territory>
                <governingAuthority>
                  <name>
                    <part codeSystem="4.33.650.1.723354.0.121.230" code="FR-ANSM" value="ANSM"/>
                  </name>
                </governingAuthority>
              </territorialAuthority>
            </primaryInformationRecipient>
          </contextOfUse>
        </component>
    <!-- ========================================================================== -->
    <!--Reference Document: Document ID -->
    <!-- eCTD EU Context of Use -->
    <!-- ========================================================================== -->
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="50C7BF17-6204-4C08-A936-CEE7746BE293"/>
            <code codeSystem="2.16.840.1.113883.3.989.0" code="eu-m1-2"/>
            <statusCode code="active"/>
        <!--Reference Document: Application Form-->
            <derivedFrom>
              <documentReference>
                <id root="4967C88D-1803-4879-9805-79EBCC17FAAB"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="80D7BF17-6204-4C08-A936-CEE7746BE172"/>
            <code codeSystem="2.16.840.1.113883.3.989.1" code="eu-m1-0"/>
```

```
            <statusCode code="active"/>
        <!--Reference Document: Cover Letter for DE -->
            <derivedFrom>
              <documentReference>
                <id root="9CF93E08-5C28-4D6D-B907-BFBE34F4119D"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="90E7BF17-6204-4C08-A936-CEE7746BE220"/>
        <!-- ================================================================= -->
        <!-- ich code = "ich-2-5" description = "m2.5 clinical overview" -->
        <!-- ================================================================= -->
            <code codeSystem="2.16.840.1.113883.3.989.3" code="ich-2-5"/>
            <statusCode code="active"/>
        <!--Reference Document: Clinical Overview -->
            <derivedFrom>
              <documentReference>
                <id root="22222222-4C2B-4570-9093-46885129AF97"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="55A7BF17-6204-4C08-A936-CEE7746BA700"/>
        <!-- ================================================================= -->
        <!-- code = "ich-3-3" description = "m3.3 literature references" -->
        <!-- ================================================================= -->
            <code codeSystem="2.16.840.1.113883.3.989.4" code="ich-3-3"/>
            <statusCode code="active"/>
        <!--Reference Document:Literature References -->
            <derivedFrom>
              <documentReference>
                <id root="33333333-7BDE-43A5-A3C8-1381E225C279"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
```

```
            <id root="66F7BF17-6204-4C08-A936-CEE7746CE400"/>
        <!-- ========================================================== -->
        <!-- code = "ich-4-3" description = "m4.3 literature references" -->
        <!-- ========================================================== -->
            <code codeSystem="2.16.840.1.113883.3.989.5" code="ich-4-3"/>
            <statusCode code="active"/>
        <!--Reference Document:Literature References 1 -->
            <derivedFrom>
              <documentReference>
                <id root="44444444-2486-484B-A6D8-D509B5A4E306"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="88B8BF17-6204-4C08-A936-CEE7746BE293"/>
      <!-- ========================================================== -->
      <!-- code = "ich-5-2" description = "m5.2 tabular listing of all clinical studies" -->
      <!-- ========================================================== -->
            <code codeSystem="2.16.840.1.113883.3.989.6" code="ich-5-2"/>
            <statusCode code="active"/>
      <!-- Reference Document:Tabular Listing of all clinical studies -->
            <derivedFrom>
              <documentReference>
                <id root="55555555-3B0E-4B61-9B6D-689A02CC8A40"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <!-- ========================================================== -->
        <!-- Reference Document : Information on the manufacturer -->
        <!-- manufacturer(s) (name, manufacturer) -->
        <!-- ========================================================== -->
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="63M8NF18-3304-4C08-C916-AA2446QE1900"/>
      <!-- ========================================================== -->
      <!-- CTD Heading - Manufacturer(s) (name, manufacturer) -->
      <!-- ich-3-2-s-2-1 - m3.2.s.2.1 manufacturer(s) - substance (R), manufacturer (R), group title (O) -->
      <!-- ========================================================== -->
            <code codeSystem="2.16.840.1.113883.3.989.7" code="ich-3-2-s-2-1"/>
            <statusCode code="active"/>
        <!-- ========================================================== -->
```

```
<!-- Reference document="Information on the manufacturer" -->
<!-- ========================================================== -->
        <derivedFrom>
          <documentReference>
            <id root="36987451-3B0E-4B61-9B6D-689A02CC8A40"/>
          </documentReference>
        </derivedFrom>
        <referencedBy typeCode="REFR">
          <keyword>
            <code codeSystem="3.26.840.1.113884.2.900.1" code="MANU001">
            <displayName value="rinkydink"/>
            </code>
          </keyword>
        </referencedBy>
      </contextOfUse>
    </component>
    <componentOf1>
      <sequenceNumber value="1"/>
<!-- ========================================================== -->
<!-- Application Submission Type : Controlled Vocabularies -->
<!-- EUTCT code = "100000155689" short name = "initial-maa" -->
<!-- Description : Initial Marketing Authorisation Application -->
<!-- ========================================================== -->
      <submission>
        <id>
          <item root="3EDF1AD3-7338-479E-9F6C-BE20E5BA95F0"/>
        </id>
        <code codeSystem="9.16.330.1.113884.2.800.2" code="initial-maa"/>
  <!-- ================================================== -->
  <!-- the contact party: a person to call if there is any questions -->
  <!-- ================================================== -->
        <callBackContact>
          <contactParty>
            <id root="12B4562-1312-31C1-2F74-1234E6789125"/>
            <code codeSystem="8.13.850.1.223354.0.121.322" code="2.4.2"/>
            <statusCode code="active"/>
            <contactPerson>
              <name>
                <part value="Pierre" type="GIV"/>
                <part value="Raynaud" type="FAM"/>
              </name>
              <telecom">
                <item value="+33155873010" capabilities="voice" use="WP"/>
                <item value="+33155873001" capabilities="fax" use="WP"/>
                <item value="pierre.raynaud@acmepharmaceuticals.com"/>
              </telecom>
```

```
            <addr">
              <part value="Paris" type="CTY"/>
              <part value="75012" type="ZIP"/>
            </addr>
          </contactPerson>
        </contactParty>
      </callBackContact>
      <subject2>
        <review>
          <id root="8C0E9431-A1CB-9832-80C3-713CEFF1M9V8"/>
          <statusCode code="active"/>
<!-- ========================================================= -->
<!-- Product name and Substance -->
<!-- ========================================================= -->
          <subject1>
            <manufacturedProduct>
              <manufacturedProduct>
                <name>
                  <part code="GF5000" value="Global Fixit"/>
                </name>
                <ingredient classCode="INGR">
                  <ingredientSubstance>
                    <name>
                      <part code="S803" value="subst1"/>
                    </name>
                  </ingredientSubstance>
                </ingredient>
              </manufacturedProduct>
            </manufacturedProduct>
          </subject1>
        </review>
      </subject2>
      <componentOf>
        <application>
          <id>
            <!-- ========================================================= -->
            <!--- procedure number FR/H/01-->
            <!-- ========================================================= -->
            <item root="5F0E8436-E1DF-4031-90D3-413DEFF109E5" extension="FR/H/01"/>
          </id>
            <!-- ========================================================= -->
<!-- Application type = New active substance (Article 8(3) of Directive N° 2001/83/EC -->
            <!-- ========================================================= -->
          <code codeSystem="eu-application-type" code="100000116047"/>
            <holder>
              <applicant>
```

```
                    <sponsorOrganization>
                      <name>
                <!-- codeSystem = OID - DUNS number -->
                        <part code="88858" value="Acme Pharmaceuticals"/>
                      </name>
                      <telecom>
                        <item value="+33155873000" capabilities="voice" use="WP"/>
                        <item value="+33155873002" capabilities="fax" use="WP"/>
                        <item value="info@acmepharmaceuticals.com"/>
                      </telecom>
                      <addr>
                        <part value="Paris" type="CTY"/>
                        <part value="75012" type="ZIP"/>
                      </addr>
                    </sponsorOrganization>
                  </applicant>
                </holder>
              <!-- ========================================================= -->
              <!-- Regulatory Authorities - countries -->
              <!-- ========================================================= -->
                    <informationRecipient>
                      <territorialAuthority>
                        <territory>
                          <code codeSystem="eu-country" code="FR"/>
                        </territory>
                        <governingAuthority>
                          <name>
                            <part language="fr" codeSystem="4.33.650.1.723354.0.121.230" code="FR-ANSM"
value="Agence Nationale de Sécurité du Médicament et des Produits de Santé"/>
                          </name>
                        </governingAuthority>
                      </territorialAuthority>
                    </informationRecipient>
                    <informationRecipient>
                      <territorialAuthority>
                        <territory>
                          <code codeSystem="eu-country" code="DE"/>
                        </territory>
                        <governingAuthority>
                          <name>
                            <part language="de" codeSystem="5.49.650.1.623351.0.121.660" code="DE-BFARM"
value="Bundesinstitut für Arzneimittel und Medizinprodukte"/>
                          </name>
                        </governingAuthority>
                      </territorialAuthority>
                    </informationRecipient>
```

```
                <informationRecipient>
                        <territorialAuthority>
                  <territory>
                    <code codeSystem="eu-country" code="BE"/>
                  </territory>
                  <governingAuthority>
                    <name>
                      <part language="fr" codeSystem="6.32.650.1.423350.0.121.350" code="BE-FAMHP"
value="Agence Fédérale des Médicaments et des Produits de Santé"/>
                    </name>
                  </governingAuthority>
                </territorialAuthority>
                </informationRecipient>
                <informationRecipient>
                  <territorialAuthority>
                    <territory>
                      <code codeSystem="eu-country" code="SE"/>
          </territory>
                  <governingAuthority>
                    <name>
                      <part language="sv" codeSystem="7.46.650.1.423350.0.121.350" code="SE-MPA"
value="Medical Products Agency"/>
                    </name>
                  </governingAuthority>
                </territorialAuthority>
                </informationRecipient>
                <informationRecipient>
                  <territorialAuthority>
                    <territory>
                      <code codeSystem="eu-country" code="UK"/>
                    </territory>
                    <governingAuthority>
                      <name>
                        <part language="en" codeSystem="8.44.650.1.423350.0.121.800" code="UK-MHRA"
value="Medicines and Healthcare products Regulatory Agency"/>
                    </name>
                  </governingAuthority>
                </territorialAuthority>
                </informationRecipient>
                  <!-- ========================================================= -->
                  <!-- Review Procedure -->
                  <!-- ========================================================= -->
              <subject8>
                  <!-- Procedure type=DCP -->
                  <!-- EUTCT code for DCP is 100000155060 short name ="DCP" -->
                  <code codeSystem="2.44.120.2.123370.0.141.879" code="DCP"/>
```

```
                </reviewProcedure>
              </subject8>
        <!-- ========================================================= -->
        <!-- common application form for all Member States involved -->
        <!-- Cover letter specific for Germany in German language -->
        <!-- ========================================================= -->
              <component>
                <document>
                  <id root="4967C88D-1803-4879-9805-79EBCC17FAAB"/>
                  <text language="en" integrityCheckAlgorithm="SHA256">
                  <reference value="m1/eu/12-form/common/common-form.pdf"/>
                  <integrityCheck>56df6492f724ee2e76e12cb4b001bd2fdc43603fb15d70afc8
9813398739fb9c</integrityCheck>
                  </text>
                  <confidentialityCode code=""/>
                </document>
              </component>
              <component>
                <document>
                  <id root="9CF93E08-5C28-4D6D-B907-BFBE34F4119D"/>
                  <text language="de" integrityCheckAlgorithm="SHA256">
                  <reference value="m1/eu/10-cover/de/de-cover.pdf"/>
                  <integrityCheck>b9a6aff775736cf100505af68da859a941432a9f9e56d245ac3eda
a4235df0ac</integrityCheck>
                  </text>
          <!-- ========================================================= -->
          <!-- Commercial Confidential Information-CCI and Protected Personal Data-PPD in the EU: -->
          <!-- L =Low -->
          <!-- M=Moderate -->
          <!-- N=Normal -->
          <!-- U=Unrestricted -->
          <!-- R=Restricted -->
          <!-- V=Very Restricted -->
          <!-- ========================================================= -->
                  <confidentialityCode code="L"/>
                </document>
    </component>
                  <!-- ========================================================= -->
                  <!-- CTD sections defined by ICH (Modules 2-5) -->
                  <!-- Document ="\..\m2\25-clin-over\clinical-overview.pdf" -->
                  <!-- Document =" \..\m3\33-lit-ref\aami-2001.pdf" -->
                  <!-- Document= "\..\m4\43-lit-ref\reference-1.pdf" -->
                  <!-- Document="\..\m5\52-tab-list\tabular-listing.pdf" -->
                  <!-- Document="\..\m3\32-body-data\32s-drug-sub\subst1-rinkydink\32s2-
manuf\manufacturer.pdf" -->
                  <!-- ========================================================= -->
```

```
            <component>
              <document>
                <id root="22222222-4C2B-4570-9093-46885129AF97"/>
                <text language="en" integrityCheckAlgorithm="SHA256">
                <reference value="m2/25-clin-over/clinical-overview.pdf"/>
                <integrityCheck>3b4f545c0e0f57c5a971c5e6015548ffa02f0f2fc9646dd28c7faa9
19b7ed06b</integrityCheck>
                </text>
              </document>
            </component>
            <component>
              <document>
                <id root="33333333-7BDE-43A5-A3C8-1381E225C279"/>
                <text language="en" integrityCheckAlgorithm="SHA256">
                <reference value="m3/33-lit-ref/aami-2001.pdf"/>
                <integrityCheck>2d7eb3613b926514cc75b8900f1b9f893d3189975942040e68b123
bbac9504d6</integrityCheck>
              </text>
              </document>
            </component>
            <component>
              <document>
                <id root="44444444-2486-484B-A6D8-D509B5A4E306"/>
                <text language="en" integrityCheckAlgorithm="SHA256">
                <reference value="m4/43-lit-ref/reference-1.pdf"/>
                <integrityCheck>58dbba78175122c32e10b593992115a8cb3eee4cf4de1d59f503e
615f2e2a568</integrityCheck>
                </text>
              </document>
            </component>
            <component>
              <document>
                <id root="55555555-3B0E-4B61-9B6D-689A02CC8A40"/>
                <text language="en" integrityCheckAlgorithm="SHA256">
                <reference value="m5/52-tab-list/tabular-listing.pdf"/>
                <integrityCheck>be7068c8ccb21d2112fb17a0e51b124fea342df8129cc173454ae1d1d
e17730a</integrityCheck>
                </text>
              </document>
            </component>
            <component>
              <document>
                <id root="36987451-3B0E-4B61-9B6D-689A02CC8A40"/>
                <text language="en" integrityCheckAlgorithm="SHA256">
                <reference value="m3/32-body-data/32s-drug-sub/subst1-rinkydink/32s2-
manuf/manufacturer.pdf"/>
```

```
                <integrityCheck>e5f61cdcac26ce21f99bc0578ce9b55e6d223566f324f05ee2a757
6ca82ab2a6</integrityCheck>
                </text>
                <confidentialityCode code="R"/>
              </document>
            </component>
          </application>
        </componentOf>
      </submission>
    </componentOf1>
  </submissionUnit>
 </subject>
</controlActProcess>
</PORP_IN000001UV>
```

Variation type 2

```
    <id root="87454521-9874-6541-1236-159842345687" />
    <code code="var-type2" codeSystem="Submission Code System OID" />
      <title value="Variation Type II" />
      <statusCode code="active" />

  - <review>
      <id />
      <statusCode code="active" />
       - <holder>
          - <applicant>
             - <sponsorOrganisation>
                - <name xsi:type="BAG_EN">
                   - <item>
                       <part value="PharmaCompany" code="888528" codeSystemVersion="OID for
Duns" />
                   </item>
                </name>
                - <telecom xsi:type="BAG_TEL">
                     <item value="tel: +33 1 55 87 31 80" use="WP" />
                     <item value="tel: +33 6 25 30 31 80" use="MC" />
                     <item value="mailto:richard.dumont@pharmacompany.com" />
                </telecom>
             - <addr xsi:type="BAG_AD">
                - <item xsi:type="AD">
                     <part type="ZIP" value="93285" />
                     <part type="STR" value="143-147 Bld Anatole France" />
                     <part type="CTY" value="Saint-Denis" />
                </item>
             </addr>
```

```
                </sponsorOrganisation>
              </applicant>
            </holder>
          - <author>
            - <territorialAuthority>
              - <territory>
                  <code code="FR" codeSystem="Country Code system OID" />
                </territory>
                - <governingAuthority>
                  - <name>
                      <part code="ANSM" value="Agence nationale de sécurité du médicament et des
produits de santé " codeSystem="Authority Code system OID" />
                    </name>
                </governingAuthority>
              </territorialAuthority>
            </author>
            - <subject2>
              - <productCategory>
                  <code code="chemical" codeSystem="ProductCategory Code system OID" />
                </productCategory>
              </subject2>
          </review>



            - <callBackContact typeCode="CALLBCK">
              - <contactParty>
                <id root="32568794-789874" identifierName="Mycontact" />
<code code="c2125" codeSystem="contactParty Event Code System OID" />
                <statusCode code="active" />
              - <contactPerson>
                - <id>
                    <item root="Globally unique contact ID" />
                  </id>
              - <name xsi:type="BAG_EN">
              - <item>
                  <part value="Richard" type="GIV" />
                  <part value="Dumont" type="FAM" />
                </item>
                </name>
              - <telecom xsi:type="BAG_TEL">
                  <item value="tel: +33 1 55 87 31 80" use="WP" />
                  <item value="tel: +33 6 25 30 31 80" use="MC" />
                  <item value="mailto:richard.dumont@pharmacompany.com" />
                </telecom>
            - <asAgent classCode="AGNT">
              - <representedOrganisation>
```

```
                - <name xsi:type="BAG_EN">
                - <item>
                  <part value="Organisation name" />
                  </item>
                  </name>
                </representedOrganisation>
            </asAgent>
        </contactPerson>
    </contactParty>
    </callBackContact>
- <component>
        <priorityNumber value="1" />
- <contextOfUse>
        <id root="12345678-1234-5678-3456-127536489712" />
          - <code code="m10cover" codeSystem="Code system OID for Cover Letter">
                <displayName value="1.0 Cover Letter" />
            </code>
           <title value="1.0 Cover Letter" />
           <statusCode code="active" />
           <setId root="set ID" />
           <versionNumber value="1.0" />
      - <primaryInformationRecipient>
          - <territorialAuthority>
              - <territory>
                    <code code="DE" codeSystem="country code system OID" codeSystemName="country code
system name" />
                </territory>
                - <governingAuthority>
                      <id root="DE-BFARM" value="BFARM" />
                  </governingAuthority>
                </territorialAuthority>
            </primaryInformationRecipient>
          - <sequelTo typeCode="RPLC">
              - <relatedContextOfUse>
                    <id root="87454521-9874-6541-1236-159842345687" />
                    <versionNumber value="1" />
                </relatedContextOfUse>
            </sequelTo>
          - <derivedFrom>
              - <documentReference>
                    <id root="12345678-1234-1234-1234-198765432198" extension="12345" />
                </documentReference>
            </derivedFrom>
          - <subjectOf>
              - <submissionReference>
                  - <id xsi:type="DSET_II">
```

```
                <item root="12345678-1234-5678-3456-127536489712" />
                </id>
              </submissionReference>
            </subjectOf>
        </contextOfUse>
    </component>
- <component>
        <priorityNumber value="1" />
- <contextOfUse>
        <id root="Context of Use ID" />
          - <code code="m12form" codeSystem="Code system OID for Application Form">
          <displayName value="1.2 application form" />
          </code>
          <title value="1.2 application form" />
          <statusCode code="active" />
          <setId root="set ID" />
          <versionNumber value="1.0" />
        - <primaryInformationRecipient>
....
          </primaryInformationRecipient>
            - <derivedFrom>
                - <documentReference>
                  <id root="12121212-1234-1234-1234-98765432198" extension="23456" />
              </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
- <componentOf>
```

APPENDIX 3 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.
Procedure	A Community registration procedure for the authorisation of medicinal products in the European Community. There are 4 types of procedure 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	See ICH eCTD IG
Payload	See ICH eCTD IG

Appendix 4 References

[This section will include references to procedures described in the IG (e.g., The SHA256 Message-Digest Algorithm).