EU Module 1 Specification

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0.92	http://esubmission.eudra.org	
0.95.1	http://esubmission.eudra.org	
0.95.2	http://esubmission.eudra.org	
0.95.3	http://esubmission.eudra.org	
1.0	http://pharmacos.eudra.org/F2/eudralex/vol-2/home.htm	
1.1		
1.2		
1.2.1	http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm	
1.3	http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm	
1.4	http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm	
1.4.1	http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm	

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Glossary of Terms

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 ***sequences***. 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 a 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 or Sequence	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**.

Introduction

This document specifies Module 1 of the electronic Common Technical Document (eCTD) for the European Union ("EU").

This document should be read together with the ICH eCTD Specification to prepare a valid eCTD submission in the EU. The latest version of the ICH eCTD Specification can be found at: http://estri.ich.org/eCTD.

EU Module 1: Regional Information

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 specified 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 for an initial submission:

- a cover letter,
- a comprehensive table of contents[1],
- an application form,
- product information documents,
- information on the experts,
- specific requirements for different types of applications (if required),
- an 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 such as answers to regulatory questions, rationale for variations and renewal documentation could also be included in Module 1.

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 document need be included in Module 1. Consult the various legal documents for guidance on the exact documents to be submitted in such a case, e.g. Regulation (EC) No 1084/2003 and Regulation (EC) No 1085/2003 for Type IA, Type IB and Type II variations.

This document describes only the region-specific information that is common to all submissions in the different Member States. However, at the same time the EU Module 1 Specification allows for country-specific information to be included in Module 1, if required. Country-specific information could relate to the details of the business process applied (e.g. specifying the number and names of those parts for which a paper copy is still requested) and local preferences for file formats.

Note that the acronym 'EMEA' will continue to be used when referring to the European Medicines Agency in various technical text herein, e.g. envelope, until such time there is a major revision to this specification.

Regional File Formats

Module 1

The file formats that can be included in Module 1 are given in Table 1. In addition to the common format PDF, as defined by the ICH eCTD Specification Document, XML and image formats are also accepted on an ad hoc basis. Note that all PDF files included in an eCTD (irrespective of the module)

[1] TOC not required for eCTD as the XML backbone acts as a table of contents

should be v1.4 or v1.7 (see ICH Q&A for further detail re pdf version acceptability), except where there is an agency-specific requirement for a later version (e.g. for an application form).
Although the use of the file formats defined in Table 1 is strongly recommended, regulatory authorities and applicants could agree on the use of other formats in Module 1. For example, proprietary format MS Word is requested by some agencies for Product Information documents in Section 1.3. These documents, if requested, should not be referenced in the eCTD backbone, and should normally be provided in addition to the PDF versions (Note: Tracked change Product Information provided in Word format is not required to be provided in PDF format within the eCTD). Guidance should be referred to regarding the provision of MS Word and other requested documents (e.g. the TIGes harmonised eCTD guidance).

Table 1 Acceptable file formats for Module 1

Document	File Format	Remark
Cover letter	XML*, 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 as the hard paper copy, if required by the receiving agency, contains the legally binding signature.
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.

* = In line with the general principles of the ICH eCTD Specification, it is intended that XML will eventually become the sole submission format for administrative forms and product information documents (as they contain structured data and a long-term goal of this development is the normalisation of data in Module 1). Note that as XML documents become available for practical implementation (including documents other than the above), they will be introduced into Module 1 and the current file formats may ultimately be replaced (after an appropriate transition period).

** = SmPC, Package Leaflet and labelling

Modules 2 to 5

No additional file formats are defined for Modules 2 to 5 other than those mentioned in the ICH eCTD Specification Document. In line with the statement on regional use of other formats in the ICH eCTD Specification Document, individual Member States and pharmaceutical companies could agree on a case-by-case basis to use formats other than the common formats. However, the use of formats other than those specified by the ICH eCTD Specification Document is discouraged.

Use of Electronic Signatures

The use of advanced electronic signatures (digital signatures) will be crucial in achieving pure electronic communication between the pharmaceutical industry and regulatory agencies, particularly for authentication of electronic submissions and documents contained therein. The EU is therefore developing a long-term strategy to implement digital signatures. Currently however, the use of digital signatures for electronic submissions within the EU is not fully supported and digital signatures should therefore not be used. Please refer to the TIGes Harmonised eCTD Guidance for information on the use of electronic signatures.

Handling of Empty or Missing eCTD Sections

For new applications (including generic applications), detailed statements justifying the absence of data or specific CTD sections should be provided in the relevant Quality Overall Summary and/or Non-Clinical/Clinical Overviews (Module 2.3, 2.4, 2.5). Note that placeholder documents highlighting 'no relevant content' should not be placed in the eCTD structure, as these would create a document lifecycle for non-existent documents, and unnecessary complication and maintenance of the eCTD.

For a generic application, there is no need to provide a justification for content that is typically absent.

The EU Module 1 is provided with a standard style-sheet that can be used to view the content. Note that the style-sheet has been designed to display the complete Module 1 table of contents (i.e. all the sections), irrespective of whether files are actually present in those sections or not.

Updating backbone attributes/metadata

It is not possible to update XML backbone attributes such as ‘manufacturer’ during the eCTD lifecycle, nor is it necessary to attempt workarounds such as deleting existing documents and resubmitting them with new attributes. The recommendation is to retain the obsolete entry and to rely on the document content to explain the current details. The sole exception to this rule is the EU envelope “submission type” attribute, which can be updated to support a mid-lifecycle change in submission type from one variation type to another (under the variation regulation). As the submission type is likely to change in any case with each submission (e.g. from ‘initial-maa’ to ‘supplemental information’ etc), this *particular* significant change in submission type should be further signalled using the free-text “submission description” envelope element.

Whilst the need for a change to the set of EU Module 1 XML attributes/metadata (this covers country, language and product information type) in the middle of the procedure is deemed to be very rare, it is recommended to contact the agency whether such change could be done during the procedure, along with other changes, or as part of an eCTD “reformat” submission.

General Architecture of Module 1

The EU Module 1 architecture is similar to that of Modules 2 to 5 of the eCTD, comprising a directory structure and a backbone with leaves. The backbone must be a valid XML document according to the EU Regional Document Type Definition (DTD). The backbone instance (the “eu-regional.xml” file) contains meta-data for the leaves, including pointers to the files in the directory structure. In addition, the EU Regional DTD defines meta-data at the submission level in the form of an envelope. The root element is “`eu-backbone`” and contains two elements: “`eu-envelope`” and “`m1-eu`”.

The EU Regional DTD is modularised, i.e. the envelope and leaves are referenced from the main part of the DTD as external entities called respectively "**`eu-envelope.mod`**" and "**`eu-leaf.mod`** ". The EU ”`leaf`” is identical to the leaf element described in the ICH eCTD DTD; reference is made to Table 6-8 of the ICH eCTD Specification. A full description of the EU Regional DTD can be found in Appendix 3 of this specification.

Examples of XML coding for a simple new application, supplemental information and a submission for a National or Mutual Recognition Procedure are provided as an annex to this specification. Examples of XML coding that support the new variation regulation are provided as well.

Files can be referred to across modules (e.g. from Module 1 to Module 2) or across sequences within the same eCTD application; note however that it is not possible to refer to files in sequences in other eCTD applications. When referring to files across modules or across sequences, the reference must always be relative, starting from the location of the XML file. For instance, a reference from within Module 1 of Sequence 0003 (e.g. 0003/m1/eu/eu-regional.xml) to a file located in Module 2 of Sequence 0000 (e.g. file “introduction.pdf” in folder 0000/m2/22-intro), would be encoded in the EU Module 1 as “../../../0000/m2/22-intro/introduction.pdf”. (This example is not business-specific – it merely serves to demonstrate the principle).

Envelope

The “eu-envelope” element is designed to be used for all types of submissions (initial, variations, renewals, etc.) for a given medicinal product and will mainly be used for the first simple processing at the agency level. The envelope provides meta-data at the submission level. A description of each "envelope" element is provided in Appendix 1 of this specification.

For Centralised Procedure submissions, the “eu-envelope” element should contain a single “envelope “element with the country attribute value set to ‘emea’. For all other procedures, the “eu-envelope” element should contain a separate “envelope” element for each Member State involved in the procedure that is going to receive that particular sequence, and each envelope country attribute should be set to the country value of the receiving Member State. Note that the value 'common' cannot be used in the envelope.

The envelope element submission ‘mode’ should only be used in variation or line extension regulatory activities, and the value can be set to: ‘single’, ‘grouping’ or ‘worksharing’. An additional high-level submission number should also be provided in the envelope under the following circumstances:

- For worksharing submissions
  Here, the submission ‘mode’ value will be ‘worksharing’ and the high-level number is a worksharing number;

- For submissions of grouped Type 1A variations that affect multiple marketing authorisations
  Here, the submission ‘mode’ will be ‘grouping’ and the high-level number is group number/‘periodic report’ number. Please refer to the annex and associated guidance for further details of this high-level number.

Such a high-level number, if appropriate, should be provided in addition to the usual product-specific tracking numbers. If the high-level number is required but is not known (e.g. for the first submission of the procedure), this element should be populated with the value ‘to be advised’. The relevant number will usually be provided by or obtained from the appropriate tracking system or regulatory agency.

Examples of ‘single’, ‘grouping’ and ‘worksharing’ submissions are provided in the annex to this specification.

m-1-eu

The “m1-eu” element of the EU regional DTD is based on the same conceptual approach as the common part of the ICH eCTD DTD. It provides an XML catalogue with meta-data at the leaf level including pointers to the location of files in a directory structure. As for the ICH eCTD DTD, the “m1-eu” element maps to the directory structure. (There may at times be what is seen to be an apparently 'redundant' directory structure, but this is necessary in order to be able to use the same file / directory structure for all procedures.) Furthermore, as the same structure will be used during the lifecycle of the submission, the use of country directories even to place a single file in one submission is justified because it could be used to house several files in a subsequent submission, and in doing so the structure would not change. A tabular overview of the directory structure explaining where to place country and language-specific files is provided in Appendix 2 of this specification.

Directory / File Structure

The EU Module 1 Specification provides a directory and file structure that is strongly recommended:

- The same high-level directory structure is used for all 4 procedures (MR, National, Decentralised and Centralised Procedures). This is possible, despite the fact that files for the MR, Decentralised and National Procedures are usually country-specific, whereas files for the Centralised Procedure are usually language-specific.
- Country directories are named according to Appendix 2.1.
- Language directories are named according to Appendix 2.2.
- The recommended directory structure for the use of country and language identifiers is described in Appendix 2. In general, Modules 1.0, 1.2, 1.3.2, 1.3.3, 1.3.4, 1.3.5, 'Additional Data' and 'Responses' have country subdirectories. Module 1.3.1 (Product Information) has both country and language subdirectories.
    - For the Centralised Procedure, the country subdirectory is always named "emea", irrespective of whether it contains "common" or country folders; language subdirectories in Module 1.3.1 have the appropriate language identifier.
    - For MR, Decentralised and National Procedures:
        - Documents for each country are placed in an appropriately named subdirectory. The folder name "common" should only be used for documents potentially applicable to all EU countries, irrespective of whether they are currently involved in the procedure or not.
        - In Module 1.3.1, every document should be placed in an appropriately named language subdirectory, even if the country only has one official language. Where a country has more than one official language (e.g. Belgium) separate language subdirectories should be used for each set of documents in a different language.
        - Should a country have documents in more than one language in a Module other than 1.3.1, then it is recommended to use the VAR (variable) part of the filename to identify the language of the document.

Node Extensions

Node extensions are a way of providing extra organisational information to the eCTD. The node extension should be visualised as an extra heading in the CTD structure and should be displayed as such when the XML backbone is viewed.

However, the use of node extensions should be limited to those areas where it is critical. Consideration should be given regarding the impact of the view for the reviewer since the inconsistent use of node extensions can lead to unanticipated effects in the cumulative view of a submission.

The following rules govern the use of node extensions in the EU:

- Node extensions must not be used where ICH-specified sub-headings already exist (e.g. indication, manufacturer, drug substance, drug product are all-ICH specified node extensions).
- Node extensions must only be used at the lowest level of the eCTD structure (e.g. a node extension can be used at the level 5.3.5.1 but must not be used at the level 5.3).
- Node extensions are mainly to be used to group together documents made up of multiple leaf elements (e.g. a clinical study made up of separate files for the synopsis, main body and individual appendices could be grouped together under a node extension with the Study Identifier as its Title attribute).
- Node extensions must be maintained over the entire life of the eCTD lifecycle (e.g. if a node extension is used in Sequence 0000 to group files for a study report in Module 5.3.5.1, then any files submitted in a later sequence must also be placed under a node extension, even if only one file is submitted).
- Node extensions may be nested as this is allowed by the eCTD DTD. However, as noted in Bullet 2, the first node extension must be at the lowest level in the eCTD structure (e.g. in Module 5.3.7 a node extension may be added to group together files with the Study Identifier as Title attribute). Further node extensions may be added as children of the Study Identifier node, separating CRFs from individual patient listings.

- The content associated with a node extension can be placed in a separate sub folder in the submission; this is recommended for studies in Module 5 where study reports are provided as multiple files. However, there is no specific requirement for an additional subfolder. For example, if node extensions are used to further define 'm1-responses', additional folders under 'm1/eu/responses/cc' are not recommended as these would then break EU file and folder naming convention rules (see next section).

File Naming Convention

File names in Module 1 follow one of two conventions.

Country-specific items in sections *1.0; 1.2; 1.3; m1-responses* and *m1-additional-data* have the general structure CC-FIXED-VAR.EXT, where CC is a country code used in some CTD modules, FIXED is a defined component of the filename based on the CTD section and VAR is an additional optional variable component. EXT represents the file extension. Components are separated by a hyphen (except the dot for the file extension). No spaces should be used within each component but hyphens can be used in the variable part to separate several words.

Fixed components are highly recommended. The variable component is optional and should be used as appropriate to further define these files. The variable component, if used, should be a meaningful concatenation of words with the option of hyphens for separators and should be kept as brief and descriptive as possible. File extensions in line with this specification should be applied as applicable.

The first component in a file name should be the country code, as per Appendix 2.1, except when the document is valid for all countries in all procedures, as per Appendix 2. The second component should be the document type code, as per Appendix 2 and 2.3. The third component if necessary should be the variable component. In cases where differentiation is needed (e.g. between 1.5mg and 15mg). the word 'point' written in full (i.e. '1point5mg') or a hyphen can be used (i.e.'1-5mg').

There are no recommendations for variable components in this specification. The format of the file is indicated by the file extension. File names should always be in lowercase, in line with the ICH eCTD specification.

Examples:

fr-cover.pdf
be-form.xml
it-form-annex1.pdf
pt-form-proofpayment.pdf
uk-outer-tablet10mg.pdf
emea-combined-tablet1-5mg.pdf
emea-combined-tablet10mgannotated.pdf
nongmo.pdf

Non-country specific items in Sections *1.4; 1.5; 1.6; 1.7; 1.8; 1.9 and 1.10* have fixed file names, as defined in Appendix 2.

Folder and File Name Path Length

The overall folder and file name path length starting from the sequence number should not exceed 180 characters, for any file in any module. This is an EU regional requirement, and it is acknowledged that this is less than the ICH agreed overall path length.

Business Protocol

It is clear that the detailed business process between industry and a regulatory agency in the EU cannot be completely harmonised due to the differences in organisation and processes. The exact description has to be provided by the individual Member States. However, a few common steps can be identified, taking into consideration that for some period of time the exchange of regulatory information will take place through exchange of physical media like CD-Rs:

1. The actual submission of the physical media on which the application is contained should be accompanied by at least a signed paper copy of the cover letter (where required by the local

agency). The content of this cover letter is defined in the ICH eCTD Specification Document Appendix 5, as is the packaging of the media units.

2. Most agencies and the EMA are unable to provide positive feedback of technically valid submissions. However, if there is any problem experienced during the upload of the sequence agencies will promptly inform the applicants.

A unique identifier of the submission is necessary and there could be different procedures for agencies to assign such a number. Either the applicant could request it of the relevant agency before submission, or, after receipt of the first submission, the agency could send it to the applicant (e.g. through an email connection for all related subsequent submissions). Relevant national guidelines should be consulted.

Change Control

The EU Module 1 specification is likely to change with time. Factors that could affect the content of the specification include, but are not limited to:

- Change in the content of the Module 1 for the CTD, either through the amendment of information, at the same level of detail, or by provision of more detailed definition of content and structure
- Change to the regional requirements for applications that are outside the scope of the CTD
- Update of standards that are already in use within the eCTD
- Identification of new standards that provide additional value for the creation and/or usage of the eCTD
- Identification of new functional requirements
- Experience of use of the eCTD by all parties, in particular Module 1.

Details of the change control process are described in an external EU document to be found at http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm

For the EU Change Control Process and Electronic Submission Change Request/Q&A Form, use the following address: http://esubmission.emea.europa.eu/doc/index.html.

Appendix 1: The EU Module 1 XML Submission

The EU Module 1 XML Submission contains an element for each Table of Contents entry of the Notice to Applicants Module 1. The following sections describe information that is captured within the Module 1 XML submission in an eCTD, but which is not captured within the Notice to Applicants Table of Contents for Module 1.

Appendix 1.1: Envelope Element Description

The "`eu-envelope`" element is the root element that defines meta-data of the submission. This element may contain several envelope entries, each related to a specific country.

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
eu-envelope		Root element that provides meta-data for the submission. This element may contain several envelopes, which are country specific.	N/A	**Mandatory**	**Unique**
envelope		Parent element for the submission meta-data. This element must be country-specific or in the case of the Centralised Procedure, 'emea'.	N/A	**Mandatory**	**Repeatable**
	country	The country to which the envelope applies (or 'emea').	**be**	**Mandatory**	**Unique**
submission		Provides administrative information associated with the submission.	N/A	**Mandatory**	**Unique**

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
	type	The type of submission material sent to the regulatory agency. The following are the valid values: ▪ `initial-maa` = Initial Marketing Authorisation Application ▪ `var-type1a` = Variation Type IA ▪ `var-type1b` = Variation Type IB ▪ `var-type2` = Variation Type II ▪ `var-nat` = National variation (e.g. national variation to apply for a pack size that is already registered within an existing MRP/DCP authorisation) ▪ `extension` = Extension ▪ `psur` = Periodic Safety Update Report (PSUR) ▪ `renewal` = Renewal (yearly or 5-yearly) ▪ `supplemental-info` = Supplemental Information (could include, for example, response to validation issues, response to questions or letter of undertaking) ▪ `fum` = Follow-Up Measure (includes post-approval commitments for national MAs) ▪ `specific-obligation` = Specific Obligation ▪ `asmf` = Active Substance Master File ▪ `pmf` = Plasma Master File ▪ `referral` = Referral under Article 29, 30, 31, 35 or 36 ▪ `annual-reassessment` = Annual Reassessment ▪ `usr` = Urgent Safety Restriction ▪ `paed-article-29` = Paediatric submission, Article 29 ▪ `paed-article-46` = Paediatric submission, Article 46 ▪ `article-58` = Article 58 (to be used for an initial application) ▪ `notification-61-3` = Notification 61(3) ▪ `transfer-ma` = Transfer of a marketing authorisation ▪ `corrigendum` = Correction to the published annexes (usually shortly after approval) ▪ `lifting-suspension` = Lifting of a suspension ▪ `withdrawal` = Withdrawal of a marketing authorisation (during any assessment use “supplemental-info”) ▪ `reformat` = Intended to support the reformatting of an existing submission dossier from any format to eCTD, i.e. a baseline eCTD submission containing no content change and which will not be subject to review (see example below) N.B. Officially, Roman numerals are used for variations, e.g. Type IA, Type II – the elements must remain Arabic, however.	var-type2	**Mandatory**	**Unique**

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
	mode	The high-level handling of the information submitted as part of variation(s) and extension applications. The mode 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 values: ▪ `single` = a single regulatory activity (e.g. a Type II variation) ▪ `grouping` = a grouped activity (e.g. several variations grouped into a single submission, or a periodic report of type IA variations applicable to one or more marketing authorisations) ▪ `worksharing` = an activity subject to a worksharing agreement (e.g. a Type II variation applicable to more than one marketing authorisation) This information should be identical with the information provided/ticked in the application form.	single	**Optional** *(note that this element must be populated for sequences in variation and line extension activities)*	**Unique**
number		This is the high-level submission number, either a 'worksharing' number, or the high-level submission number to be used when grouping Type IA variations for multiple marketing authorisations (Note that for submissions affecting multiple MAs, the 'xxxx' used in the submission number is a permanent placeholder, as a single product number cannot be provided). If the Applicant did not obtain the sequential number from the relevant Authorities in advance of their application this field should be populated as "xxxx" as well.	For worksharing: **EMEA/H/xxxx/WS/001** **For grouped IAs:** **EMEA/H/C/xxxx/IG/xxxx**	**Optional**	**Unique**
tracking		Provides administrative information associated with the application.	N/A	**Mandatory**	**Unique**

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
number		This is any number, used by an agency or the applicant to track the submission, in any procedure, in relation to a particular product. This could be one or more of the following: • an MRP/DCP number (e.g. `DE/H/0126/001/MR`), • a national procedure number (e.g. `2131577`), • the EMEA application number (e.g. `EMEA/H/C/000123` or `EMEA/H/C/000123/II/14`), • an authorisation or licence number, (e.g. `EU/1/00/44/0003 – 0004`) • any other number used by an agency to track a submission, (e.g. `PL01234/0003-0004`) • a number used by the applicant to manage the submission within their company (e.g. `Pharmacompany123`) There must be at least one tracking number identified from the regulators and, in addition, the applicant can choose to include an internal tracking number. It is suggested that if the procedure number has not yet been allocated by the agency then the term 'to be advised' should be used. Applicants should consult national guidance for further information. In case of worksharing, or grouped type IA variations applying to more than one MA, a separate eCTD submission must be built for each MA covered by the variation. In the envelope of each of the eCTD submissions, the high-level submission number will be the same, but the individual tracking numbers listed here should be specific to the MA in question, e.g.: For worksharing: • `EMEA/H/C/000123/WS005/` For grouped type 1A variations across multiple MAs: • `EMEA/H/C/000123/IG003/` Please ensure that these WS/IG numbers are always mentioned in the case of supplemental information or corrigendum otherwise the Agency might not be able to process your submission correctly.	See column left	**Mandatory**	**Repeatable**
applicant		The name of the company submitting the eCTD.	**PharmaCompany Ltd.**	**Mandatory**	**Unique**

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
agency		Parent element for the identification of the receiving agency.	N/A	**Mandatory**	**Unique**
	code	The identification of the receiving agency (see Appendix 2.4).	**EU-EMEA**	**Mandatory**	**Unique**
procedure		Defines the procedure in use with the submission	N/A	**Mandatory**	**Unique**
	type	The type of procedure for the submission. The following are the valid values: ▪ `centralised` = Centralised Procedure ▪ `national` = National Procedure ▪ `mutual-recognition` = Mutual Recognition Procedure ▪ `decentralised` = Decentralised Procedure	**centralised**	**Mandatory**	**Unique**
invented-name		The name of the medicinal product.	**WonderPill**	**Mandatory**	**Repeatable**
inn		International Non-proprietary Name, used to identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A non-proprietary name is also known as a generic name.	**Pioglitazone hydrochloride**	**Optional**	**Repeatable**
sequence		This is the sequence number of the submission – this should start at 0000 for the initial submission, and then increase incrementally with each subsequent submission related to the same product e.g. 0000, 0001, 0002, 0003 etc.	**0000**	**Mandatory**	**Unique**
related-sequence		This is the sequence number of previous submission(s) to which this submission relates e.g. the responses to questions to a particular variation.	**0001** see guidance below on use and the annex	**Optional**	**Repeatable**
submission-description		This element is used to provide a free text description of the submission. The list below provides additional examples for such a field: ▪ For an MAA: Original MAA Application for <Product X> / Response to D120 LOQ ▪ For a Type II variation: Please quote the scope of variation from the Application Form ▪ For a Type IB variation: Please quote the scope of variation from the Application Form ▪ For an Annual Reassessment submission: 4th AR submission for <Product X> ▪ Response to validation questions ▪ Providing supplementary information ▪ Dxxx translations	**Response to D120 LOQ**	**Mandatory**	**Unique**

Example of the use of the Related Sequence

The Related Sequence number is used to identify sequences belonging to the same ‘regulatory activity’. A 'regulatory activity' is a logical unit of submission activity (e.g., a Type II Variation) with a defined start and end point (e.g. initial submission to final approval). In the eCTD world, this will consist of all the sequences that together make up the lifecycle of that particular 'regulatory activity’.

The related sequence attribute should always be left blank for new applications or new regulatory activities (e.g. variations, PSURs). When submitting lifecycle sequences within an existing activity, the related sequence attribute should be populated with the sequence number of the first sequence in the activity, regardless of how many sequences make up the activity. The related sequence attribute should be considered independent of any modified file attributes in a submission. For example, if a sequence 0010 modifies files (leaves) in sequence 0008 and 0009, the entry for related sequence in sequence 0010 should be the sequence number that started the regulatory activity that 0010 falls within, which will not necessarily be sequence 0008 or 0009. See below for some illustrative examples.

It is generally expected that there is usually just one Related Sequence, but there are occasions where more than one Related Sequence should be provided: e.g. there are two FUMs (sequence 0050 and sequence 0060) and a single response (sequence 0070) is produced that relates to both FUMs. If more than one different category of activities are referred to (as related sequence), then the “highest category” should be used in the envelope attributes, and if any of the related variations were grouped, then ‘grouping’ should be used.

Special attention should be paid to the correct use of the Related Sequence element when the regulatory activity is a variation that covers more than one Marketing Authorisation. An example is given in the Annex.

Sequence	Submission description	Related sequence	Comment
0000	Original MAA application	<none>	
0001	Day 121 Responses to questions on the original application	0000	This is a continuation of the regulatory activity initiated in 0000 and so the related sequence points to the beginning of that activity
0002	Day 181 Responses to further questions on the original application	0000	This is a continuation of the regulatory activity initiated in 0000 and so the related sequence points to the beginning of that activity
0003	Letter of Undertaking (submission type: supplemental information)	0000	This is a continuation of the regulatory activity initiated in 0000 and so the related sequence points to the beginning of that activity
0004	Type II variation for ‘Treatment of Pain’ indication	<none>	This is the beginning of a new regulatory activity and so no related sequence is included
0005	Type II variation for a change in manufacturing site (Westferry)	<none>	This is the beginning of a new regulatory activity and so no related sequence is included
0006	Responses to questions on Type II variation for ‘Treatment of Pain’ indication	0004	This is a continuation of the regulatory activity initiated in 0004 and so the related sequence points to the beginning of that activity
0007	Responses to questions on Type II variation for change in	0005	This is a continuation of the regulatory activity initiated in 0005 and so

Sequence	Submission description	Related sequence	Comment
	manufacturing site (Westferry)		the related sequence points to the beginning of that activity
0008	Extension to introduce a new dosage form (iv solution) that amends information provided in the original application and the manufacturing change variation	<none>	This is the beginning of a new regulatory activity and so no related sequence is included
0009	Updated, agreed, product information taking into account new indication ('Treatment of Pain')	0004	This is the completion of the new indication ('Treatment of Pain') activity
00010	Updated, agreed product information for the iv formulation	0008	This is the completion of the new dosage form (iv solution) activity

For a new Regulatory Activity, the appropriate submission type should be used. Applicants should refer to the submission type descriptions in the EU Module 1 specification. For the sequence that initiates a Regulatory Activity 'supplemental-info' and 'corrigendum' should not be used. These should only be used for subsequent sequences within that Regulatory Activity.

The submission type 'supplemental-info' should be routinely used for all subsequent sequences until the conclusion of the Regulatory Activity. The submission type 'corrigendum' should only be used in exceptional circumstances to correct information, typically for product information, after the Regulatory Activity has concluded.

Tables 1, 2 and 3 provide examples of this convention.

Table 1: Example of an initial MAA in the Centralised Procedure

Sequence number	Submission Description	Submission Type	Related Sequence
0000	Initial MAA	initial-maa	none
0001	Validation update	supplemental-info	0000
0002	Day 121 responses	supplemental-info	0000
0003	Day 181 responses	supplemental-info	0000
0004	Day 210 Agreed English product information	supplemental-info	0000
0005	Day 215 – translated product information	supplemental-info	0000
0006	Final translations of product information for Decision	supplemental-info	0000
0007	Correction of errors in Danish product information after Decision	corrigendum	0000

Table 2: Example of an initial MAA in the Decentralised Procedure

Sequence number	Submission Description	Submission Type	Related Sequence
0000	Initial MAA	initial-maa	none
0001	Validation update	supplemental-info	0000
0002	Day 106 responses	supplemental-info	0000
0003	Day 180 responses	supplemental-info	0000
0004	Day 210 Agreed English product information	supplemental-info	0000

Table 3: Example of a Variation

Sequence number	Submission Description	Submission Type	Related Sequence
0008	Variation for new indication of COPD	var-type2	none
0009	Validation update	supplemental-info	0008
0010	Responses to questions	supplemental-info	0008

Table 4 provides details of which submission types should never have a related sequence and which should always have a related sequence

Table 4: List of Submission Types and the Use of Related Sequence

Submission Type	Should Never Have A Related Sequence	Should Always Have A Related Sequence
initial-maa	Yes	
var-type1a	Yes	
var-type1b	Yes	
var-type2	Yes	
var-nat	Yes	
extension	Yes	
psur	Yes	
renewal	Yes	
supplemental-info		Yes
fum	Yes	
specific-obligation	Yes	
asmf	Yes	

Submission Type	Should Never Have A Related Sequence	Should Always Have A Related Sequence
pmf	Yes	
referral	Yes	
annual-reassessment	Yes	
usr	Yes	
paed-article-29	Yes	
paed-article-46	Yes	
article-58	Yes	
notification-61-3	Yes	
transfer-ma	Yes	
corrigendum		Yes
lifting-suspension	Yes	
withdrawal	Yes	
reformat	Yes	

Example of the use of the submission type ‘reformat’

The submission type ‘reformat’ should be used in each case. (Note: the submission type ‘supplemental-info’ should not be used for the second reformat submission.) Related sequence should not be used.
An example is given below.

Sequence number	Submission Description	Submission Type	Related Sequence
0000	Baseline of Modules 4 & 5	reformat	None
0001	Variation for new indication of COPD	var-type2	None
0002	Baseline of Module 3	reformat	None
0003	Extension for 8mg tablet	extension	None

Appendix 1.2: Country-Specific Elements

A number of the elements that represent NtA Module 1 TOC headings possess the child element "`specific`", which allows country-specificity of content to be explicitly indicated.

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
specific		Parent element for identifying the receiving country for a document or documents.	N/A	Mandatory	Repeatable
	country	The receiving country for the document(s) (or "common") (see Appendix 2.1 for full list of allowable values)	uk	Mandatory	Unique

Module 1 elements that have "specific" child elements can therefore contain multiple documents, each with content for review by a different country. These elements are listed below:

- `m1-0-cover` (1.0 Cover Letter)
- `m1-2-form` (1.2 Application Form)
- `m1-3-2-mockup` (1.3.2 Mock-Up)
- `m1-3-3-specimen` (1.3.3 Specimen)
- `m1-3-4-consultation` (1.3.4 Consultation with Target Patient Groups)
- `m1-3-5-approved` (1.3.5 Product Information Already Approved in the Member States)
- `m1-responses` (Responses to Questions)
- `m1-additional-data` (Additional Data)

Appendix 1.3: Product Information Element Description

The "`m1-3-1-spc-label-pl`" corresponds to the Notice to Applicants heading 1.3.1 SmPC, Labelling and Package Leaflet. This element can have multiple child "`pi-doc`" elements that allow identification of product information language, document type and applicable country as described below.

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
pi-doc		Parent element for identification of the type, language and country of one or more product information documents.	N/A	Mandatory	Repeatable
	xml:lang	The language that the product information is written in (see Appendix 2.2 for allowable values).	fr	Mandatory	Unique
	type	The type of product information document (see Appendix 2.3 for allowable values).	combined	Mandatory	Unique

	country	The receiving country for the product information (or “common”) (see Appendix 2.1 for full list of allowable values)	be	Mandatory	Unique

Appendix 2: Directory / File Structure for Module 1

The directory / file structure is defined in this appendix as a table containing the following information:

Sequential number		Each item in the table has a unique sequentially assigned reference number. These reference numbers can change with each version of this appendix.
	Number	CTD section number
	Title	CTD title
	Element	Element name in the EU Backbone
	File/Directory	File/Directory name from m1/eu – should be relative path from eu/m1 e.g. 12-form/fr-form.pdf. This is consistent with ICH standards. The file extension corresponds to the file type; i.e. the “pdf” extension is only illustrative.
	Comment	Comments

Where the following conventions are used:

Codes*	**Definition**
CC	Country Code, also referred to as the destination code as per Appendix 2.1
LL	Local Language code as per Appendix 2.2
EXT	File extension.
PIDOC	Product Information Document identifier as per Appendix 2.3
VAR	Variable component of the filename.
DDDD	A sequence number made of 4 digits (e.g. 0000)

* = The names of the actual files and directories used should be presented in lower case in accordance with the eCTD specification. The use of upper case for codes is for illustrative purposes only to show differentiation between the variable parts and the fixed part of the name.

1	Number	
	Title	Module 1 EU
	Element	m1-eu
	Directory	m1/eu
	Comment	Top level directory for the EU Module 1as per ICH eCTD Specification
2	Number	
	Title	
	Element	
	File	m1/eu/eu-regional.xml
	Comment	The EU Regional XML instance including the envelope information. Note that the operation attribute for the eu.regional.xml should always be set to ‘new’.
3	Number	1.0
	Title	Cover Letter
	Element	m1-0-cover
	Directory	m1/eu/10-cover
	Comment	
4	Number	
	Title	
	Element	
	Directory	m1/eu/10-cover/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.

5	Number	
	Title	
	Element	
	File	m1/eu/10-cover/*CC*/*CC*-cover-*VAR*.*EXT*
	Comment	Filename for the Cover Letter composed of a fixed component "*CC*", a fixed component "cover" and an optional variable component if required (e.g. fr-cover-variationrationale.pdf). When only the cover letter is submitted in this directory the file name should be *CC*-cover.pdf. Note that the tracking table required with MPR/DCP submissions should be located within a 'common' directory, with the filename 'common-cover-tracking.pdf' or 'common-cover-tracking.xml'. Single document correspondences e.g. Letter of Undertakings should be placed here.
6	Number	1.2
	Title	Application Form
	Element	m1-2-form
	Directory	m1/eu/12-form
	Comment	The Application Form refers to any form (new applications, applications for variations or renewals).
7	Number	
	Title	
	Element	
	Directory	m1/eu/12-form/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.
8	Number	
	Title	
	Element	
	File	m1/eu/12-form/*CC*/*CC*-form-*VAR*.*EXT*

	Comment	Filename for the Application Form composed of a fixed component "*CC*", a fixed component "form" and an optional variable component to be used if required (e.g. fr-form-annex01.pdf, fr-form-proofpayment.pdf). When only the application form is submitted in this directory the file name should be *CC* -form.pdf. Annexes that potentially apply to <u>all</u> EU countries should be placed in the 'common' sub-directory (e.g. common-form-annex12.pdf, common-form-pheurcertificate.pdf). The variable component, if used, should be a logical name and should be added without spaces Supportive documents, which are not part of any M2-5 section or Response to Questions, should be placed here. Any updates to documents originating from M2-5 should replace the outdated version in its original location in M2-5. Supportive documents submitted as answers to questions should be placed in Module 1 Responses to Questions (see line 66-68).
9	Number	1.3
	Title	Product Information
	Element	m1-3-pi
	Directory	m1/eu/13-pi
	Comment	General placeholder for Product Information
10	Number	1.3.1
	Title	SmPC, Labelling and Package Leaflet
	Element	m1-3-1-spc-label-pl
	Directory	m1/eu/13-pi/131-spclabelpl
	Comment	General placeholder for SmPC, Labelling, Package Leaflet or Combined PI when submitting paper-based PI documents (PDF).
11	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/131-spclabelpl/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.
12	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/131-spclabelpl/*CC*/*LL*
	Comment	Always use a language directory at this level during the lifecycle of the submission. See Row 13 for an example.

13	Number	
	Title	
	Element	
	File	m1/eu/13-pi/131-spclabelpl/*CC*/*LL*/*CC-PIDOC-VAR*.*EXT*
	Comment	Filename for the spc-label-pl document composed by a fixed component "*CC*", a fixed component "PIDOC" as per table of Appendix 2.3 and an optional variable component to be used if needed (e.g. m1/eu/13-pi/131-spclabelpl/emea/de/emea-combined-tablet10mgde.pdf).

14	Number	1.3.1
	Title	SmPC, Labelling and Package Leaflet
	Element	m1-3-1-pim
	File	m1/eu/13-pi/131-pim-*DDDD-AR*.zip or m1/eu/13-pi/131-pim-*DDDD-AR*.tgz
	Comment	This element should not be used anymore as the PIM project was closed on 28/03/2011 and will be removed from this annex 2 and the DTD. With the next major revision of the EU M1 Specification the required technical changes will be introduced.
15	Number	1.3.2
	Title	Mock-up
	Element	m1-3-2-mockup
	Directory	m1/eu/13-pi/132-mockup
	Comment	
16	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/132-mockup/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.
17	Number	
	Title	
	Element	
	File	m1/eu/13-pi/132-mockup/*CC*/*CC*-mockup-*VAR.EXT*
	Comment	Filename for the mock-up document composed by a fixed component “*CC*”, a fixed component “mockup” and an optional variable component to be used if needed. (e.g. fr-mockup-tablet10mgouter.pdf).

18	Number	1.3.3
	Title	Specimen
	Element	m1-3-3-specimen
	Directory	m1/eu/13-pi/133-specimen
	Comment	
19	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/133-specimen/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.
20	Number	
	Title	
	Element	
	File	m1/eu/13-pi/133-specimen/CC/*CC*-specimen-*VAR*.*EXT*
	Comment	Filename for the list of physical specimens provided with the submission composed by a fixed component "*CC*", a fixed component "specimen" and an optional variable component to be used if needed. (e.g. fr-specimen.pdf).
21	Number	1.3.4
	Title	Consultation with Target Patient Groups
	Element	m1-3-4-consultation
	Directory	m1/eu/13-pi/134-consultation
	Comment	
22	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/134-consultation/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.

23	Number	
	Title	
	Element	
	File	m1/eu/13-pi/134-consultation/*CC*/*CC*-consultation-*VAR*.*EXT*
	Comment	Filename for the results of assessments carried out in cooperation with target patient groups on the package leaflet, composed by a fixed component “*CC*”, a fixed component “consultation” and an optional variable component to be used if needed. (e.g. consultation-tablet10mgpl.pdf).
24	Number	1.3.5
	Title	Product Information already approved in the Member States
	Element	m1-3-5-approved
	Directory	m1/eu/13-pi/135-approved
	Comment	
25	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/135-approved/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted.
26	Number	
	Title	
	Element	
	File	m1/eu/13-pi/135-approved/*CC*/*CC*-approved-*VAR*.*EXT*
	Comment	Filename for the approved Product Information document composed by a fixed component “*CC*”, a fixed component “approved” and an optional variable component to be used if needed. The “CC” prefix should be used for the country receiving the submission, not the country where the product information is already approved (e.g. when submitting a dossier in France, where Product Information has been approved in Poland, the file name would be (e.g. fr-approved-poland.pdf or fr-approved-polandmanumber.pdf).
27	Number	1.3.6
	Title	Braille
	Element	m1-3-6-braille
	Directory	m1/eu/13-pi/136-braille
	Comment	

28	Number	
	Title	
	Element	
	File	m1/eu/13-pi/136-braille/braille-*VAR*.*EXT*
	Comment	Filename for the Braille information is composed by a fixed component “braille” and an optional variable component to be used if needed. (e.g. braille.pdf).
29	Number	1.4
	Title	Information about the Experts
	Element	m1-4-expert
	Directory	m1/eu/14-expert
	Comment	General placeholder for Expert Information.
30	Number	1.4.1
	Title	Quality
	Element	m1-4-1-quality
	Directory	m1/eu/14-expert/141-quality
	Comment	General placeholder for quality information.
31	Number	
	Title	
	Element	
	File	m1/eu/14-expert/141-quality/quality-*VAR*.*EXT*
	Comment	Filename for the quality expert document composed by a fixed component “quality” and an optional variable component to be used if needed. (e.g. quality.pdf).
32	Number	1.4.2
	Title	Non-Clinical
	Element	m1-4-2-non-clinical
	Directory	m1/eu/14-expert/142-nonclinical
	Comment	General placeholder for non-clinical information.

33	Number	
	Title	
	Element	
	File	m1/eu/14-expert/142-nonclinical/nonclinical-*VAR*.*EXT*
	Comment	Filename for the non-clinical expert document composed by a fixed component “nonclinical” and an optional variable component to be used if needed. (e.g. nonclinical.pdf).
34	Number	1.4.3
	Title	Clinical
	Element	m1-4-3-clinical
	Directory	m1/eu/14-expert/143-clinical
	Comment	General placeholder for clinical information.
35	Number	
	Title	
	Element	
	File	m1/eu/14-expert/143-clinical/clinical-*VAR*.*EXT*
	Comment	Filename for the clinical expert document composed by a fixed component “clinical” and an optional variable component to be used if needed. (e.g. clinical.pdf).
36	Number	1.5
	Title	Specific Requirements for Different Types of Applications
	Element	m1-5-specific
	Directory	m1/eu/15-specific
	Comment	General placeholder for Specific Information.
37	Number	1.5.1
	Title	Information for Bibliographical Applications
	Element	m1-5-1-bibliographic
	Directory	m1/eu/15-specific/151-bibliographic
	Comment	General placeholder for bibliographical applications.

38	Number	
	Title	
	Element	
	File	m1/eu/15-specific/151-bibliographic/bibliographic-*VAR*.*EXT*
	Comment	Filename for the specific bibliographic submission information composed by a fixed component “bibliographic” and an optional variable component to be used if needed. (e.g. bibliographic.pdf).
39	Number	1.5.2
	Title	Information for Generic, ‘Hybrid’ or Bio-similar Applications
	Element	m1-5-2-generic-hybrid-biosimilar
	Directory	m1/eu/15-specific/152-generic-hybrid-bio-similar
	Comment	General placeholder for generic, ‘hybrid’ or bio-similar applications.
40	Number	
	Title	
	Element	
	File	m1/eu/15-specific/152-generic-hybrid-bio-similar/generic-*VAR*.*EXT* or m1/eu/15-specific/152-generic-hybrid-bio-similar/hybrid-*VAR*.*EXT* or m1/eu/15-specific/152-generic-hybrid-bio-similar/biosimilar-*VAR*.*EXT*
	Comment	Filename for the specific generic, hybrid or bio-similar submission information composed by a fixed component “generic” or “hybrid” or “biosimilar”, and an optional variable component to be used if needed (e.g. generic.pdf).
41	Number	1.5.3
	Title	(Extended) Data/Market Exclusivity
	Element	m1-5-3-data-market-exclusivity
	Directory	m1/eu/15-specific/153-data-market-exclusivity
	Comment	General placeholder for (extended) data/market exclusivity.
42	Number	
	Title	
	Element	
	File	m1/eu/15-specific/153-data-market-exclusivity/datamarketexclusivity-*VAR*.*EXT*
	Comment	Filename for the data / market exclusivity composed of a fixed component “datamarketexclusivity” and an optional variable component to be used if needed (e.g. datamarketexclusivity.pdf).

43	Number	1.5.4
	Title	Exceptional Circumstances
	Element	m1-5-4-exceptional-circumstances
	Directory	m1/eu/15-specific/154-exceptional
	Comment	General placeholder for marketing authorisation granted under exceptional circumstances.
44	Number	
	Title	
	Element	
	File	m1/eu/15-specific/154-exceptional/exceptional-*VAR*.*EXT*
	Comment	Filename for marketing authorisation granted under exceptional circumstances, composed of a fixed component “exceptional” and an optional variable component to be used if needed (e.g. exceptional.pdf).
45	Number	1.5.5
	Title	Conditional Marketing Authorisation
	Element	m1-5-5-conditional-ma
	Directory	m1/eu/15-specific/155-conditional-ma
	Comment	General placeholder for conditional marketing authorisation.
46	Number	
	Title	
	Element	
	File	m1/eu/15-specific/155-conditional-ma/conditionalma-*VAR*.*EXT*
	Comment	Filename for conditional marketing authorisation, composed of a fixed component “conditionalma” and an optional variable component to be used if needed (e.g. conditionalma.pdf).
47	Number	1.6
	Title	Environmental Risk Assessment
	Element	m1-6-environrisk
	Directory	m1/eu/16-environrisk
	Comment	General placeholder for Environmental Risk Assessment.

48	Number	1.6.1
	Title	Non-GMO
	Element	m1-6-1-non-gmo
	Directory	m1/eu/16-environrisk/161-nongmo
	Comment	General placeholder for non-GMO.
49	Number	
	Title	
	Element	
	File	m1/eu/16-environrisk/161-nongmo/nongmo-*VAR*.*EXT*
	Comment	Filename for the environmental risk assessment non-GMO composed by a fixed component “nongmo” and an optional variable component to be used if needed. (e.g. nongmo.pdf).
50	Number	1.6.2
	Title	GMO
	Element	m1-6-2-gmo
	Directory	m1/eu/16-environrisk/162-gmo
	Comment	General placeholder for GMO.
51	Number	
	Title	
	Element	
	File	m1/eu/16-environrisk/162-gmo/gmo-*VAR*.*EXT*
	Comment	Filename for the environmental risk assessment GMO-composed by a fixed component “gmo” and an optional variable component to be used if needed (e.g. gmo.pdf).
52	Number	1.7
	Title	Information relating to Orphan Market Exclusivity
	Element	m1-7-orphan
	Directory	m1/eu/17-orphan
	Comment	General placeholder for Orphan Market Exclusivity information.

53	Number	1.7.1
	Title	Similarity
	Element	m1-7-1-similarity
	Directory	m1/eu/17-orphan/171-similarity
	Comment	General placeholder for information on similarity with authorised orphan product.
54	Number	
	Title	
	Element	
	File	m1/eu/17-orphan/171-similarity/similarity-*VAR.EXT*
	Comment	Filename for the information on similarity composed by a fixed component “similarity” and an optional variable component to be used if needed.
55	Number	1.7.2
	Title	Market Exclusivity
	Element	m1-7-2-market-exclusivity
	Directory	m1/eu/17-orphan/172-market-exclusivity
	Comment	General placeholder for information on market exclusivity.
56	Number	
	Title	
	Element	
	File	m1/eu/17-orphan/172-market-exclusivity/marketexclusivity-*VAR.EXT*
	Comment	Filename for information on market exclusivity composed by a fixed component “marketexclusivity” and an optional variable component to be used if needed.
57	Number	1.8
	Title	Information relating to Pharmacovigilance
	Element	m1-8-pharmacovigilance
	Directory	m1/eu/18-pharmacovigilance
	Comment	General placeholder for information on pharmacovigilance.

58	Number	1.8.1
	Title	Pharmacovigilance System
	Element	m1-8-1-pharmacovigilance-system
	Directory	m1/eu/18-pharmacovigilance/181-phvig-system
	Comment	General placeholder for information on pharmacovigilance system.
59	Number	
	Title	
	Element	
	File	m1/eu/18-pharmacovigilance/181-phvig-system/phvigsystem-*VAR*.*EXT*
	Comment	Filename for information on pharmacovigilance system composed by a fixed component “phvigsystem” and an optional variable component to be used if needed.
60	Number	1.8.2
	Title	Risk-management System
	Element	m1-8-2-risk-management-system
	Directory	m1/eu/18-pharmacovigilance/182-riskmgt-system
	Comment	General placeholder for information on risk management system.
61	Number	
	Title	
	Element	
	File	m1/eu/18-pharmacovigilance/182-riskmgt-system/riskmgtsystem-*VAR*.*EXT*
	Comment	Filename for information on pharmacovigilance system composed by a fixed component “riskmgtsystem” and an optional variable component to be used if needed.
62	Number	1.9
	Title	Information relating to Clinical Trials
	Element	m1-9-clinical-trials
	Directory	m1/eu/19-clinical-trials
	Comment	General placeholder for information on clinical trials.

63	Number	
	Title	
	Element	
	File	m1/eu/19-clinical-trials/clinicaltrials-*VAR*.*EXT*
	Comment	Filename for information on clinical trials composed by a fixed component “clinicaltrials” and an optional variable component to be used if needed.
64	Number	1.10
	Title	Information relating to Paediatrics
	Element	m1-10-paediatrics
	Directory	m1/eu/110-paediatrics
	Comment	General placeholder for information on paediatrics.
65	Number	
	Title	
	Element	
	Directory	m1/eu/110-paediatrics/paediatrics-*VAR*.*EXT*
	Comment	Filename for information on paediatrics composed by a fixed component “paediatrics” and an optional variable component to be used if needed.
66	Number	
	Title	Responses to Questions
	Element	m1-responses
	Directory	m1/eu/responses
	Comment	
67	Number	
	Title	
	Element	
	Directory	m1/eu/responses/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.

68	Number	
	Title	
	Element	
	File	m1/eu/responses/*CC*/*CC*-responses-*VAR*.*EXT*
	Comment	Filename for responses to questions composed by a fixed component “*CC*”, a fixed component “responses” and an optional variable component to be used if needed (e.g. be-responses.pdf).
69	Number	
	Title	Additional Data
	Element	m1-additional-data
	Directory	m1/eu/additional-data
	Comment	The 'Additional Data’ section should only be used for information required for National, MR and Decentralised Procedures; it is therefore not generally applicable for the Centralised Procedure.
70	Number	
	Title	
	Element	
	Directory	m1/eu/additional-data/*CC*
	Comment	Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission.
71	Number	
	Title	
	Element	
	File	m1/eu/additional-data/*CC*/*CC*-additionaldata-*VAR*.*EXT*
	Comment	Filename for additional information requested composed by a fixed component “*CC*”, a fixed component “additionaldata” and an optional variable component to be used if needed (e.g. be-additionaldata-yellowpink.pdf). Supporting data for variations should be not be placed in this section; wherever possible they should be placed in the relevant CTD section, primarily within Module 3 ‘Quality’ and Module 1 (1.3.1) ‘Summary of Product Characteristics, Labelling and Package Leaflet’. Where documents cannot be assigned to specific CTD-defined locations, then they should be attached to the 1.2 Application Form. The same approach should be used for renewals. Additionally see comments in row no 8. The 'Additional Data’ section should only be used for information required for country specific information/documentation for National, MR and Decentralised Procedures; it is not applicable for the Centralised Procedure.

72	Number	
	Title	
	Element	
	Directory	m1/eu/util
	Comment	Additional folder to hold utility files used in EU Region only.
73	Number	
	Title	
	Element	
	Directory	m1/eu/util/dtd
	Comment	Additional folder to hold DTD files used in EU Region only.
74	Number	
	Title	
	Element	
	Directory	util/dtd
	Comment	ICH specified location for eCTD DTD files.
75	Number	
	Title	
	Element	
	Directory	util/style
	Comment	ICH specified location for eCTD style-sheet files. The style-sheet to be used should be the most recent version, which is always published as part of the specification package for download. Note that the XML instance can only point to one style-sheet and that referencing a customised style-sheet will effectively prevent the agency using the official one. It is therefore recommended not to submit customised style-sheets.

Appendix 2.1: Destination Codes

In most cases the destination code is an ISO-3166-1-alpha-2 code usually called “country code” or “*CC*” in this specification.

Code	Destination	Comment
at	Austria	ISO-3166-1-alpha-2 code
be	Belgium	ISO-3166-1-alpha-2 code
bg	Bulgaria	ISO-3166-1-alpha-2 code
common	All countries	This is not an ISO code, but should be used to identify documents that are potentially applicable to all EU countries, irrespective of whether they are participating in the procedure or not This code should be used in the Decentralised Procedure and Mutual Recognition Procedures only.
cy	Cyprus	ISO-3166-1-alpha-2 code
cz	Czech Republic	ISO-3166-1-alpha-2 code
de	Germany	ISO-3166-1-alpha-2 code
dk	Denmark	ISO-3166-1-alpha-2 code
ee	Estonia	ISO-3166-1-alpha-2 code
el	Greece	This is not an ISO code, but should be used as per guidance for application forms in the Notice to Applicants
emea	EMEA	This is not an ISO code, but should be used for files that apply to all countries in the Centralised Procedure
es	Spain	ISO-3166-1-alpha-2 code
fi	Finland	ISO-3166-1-alpha-2 code
fr	France	ISO-3166-1-alpha-2 code
hu	Hungary	ISO-3166-1-alpha-2 code
ie	Ireland	ISO-3166-1-alpha-2 code
is	Iceland	ISO-3166-1-alpha-2 code
it	Italy	ISO-3166-1-alpha-2 code
li	Liechtenstein	ISO-3166-1-alpha-2 code
lt	Lithuania	ISO-3166-1-alpha-2 code
lu	Luxembourg	ISO-3166-1-alpha-2 code
lv	Latvia	ISO-3166-1-alpha-2 code
mt	Malta	ISO-3166-1-alpha-2 code
nl	Netherlands	ISO-3166-1-alpha-2 code
no	Norway	ISO-3166-1-alpha-2 code
pl	Poland	ISO-3166-1-alpha-2 code
pt	Portugal	ISO-3166-1-alpha-2 code
ro	Romania	ISO-3166-1-alpha-2 code
se	Sweden	ISO-3166-1-alpha-2 code
si	Slovenia	ISO-3166-1-alpha-2 code
sk	Slovakia	ISO-3166-1-alpha-2 code
uk	United Kingdom	This is not an ISO country code, but should be used as per guidance for application forms in the Notice to Applicants

Appendix 2.2: Language Codes

Codes are ISO-639-1 codes defining the European languages used in the context of eCTD submissions for marketing authorisation applications in the EEA.

Code	Language
bg	Bulgarian
cs	Czech
da	Danish
de	German
el	Greek
en	English
es	Spanish
et	Estonian
fi	Finnish
fr	French
hu	Hungarian
is	Icelandic
it	Italian
lt	Lithuanian
lv	Latvian
mt	Maltese
nl	Dutch
no	Norwegian
pl	Polish
pt	Portuguese
ro	Romanian
sk	Slovakian
sl	Slovenian
sv	Swedish

Appendix 2.3: SmPC, Labelling and Package Leaflet File Name Identifiers

PI DOC	Description
spc	Summary of Product Characteristics
annex2	Annex II
outer	Outer Packaging
interpack	Intermediate Packaging*
impack	Immediate Packaging
other	Other product information
pl	Package Leaflet
combined	Single text file incorporating the following documents: spc + annex2 + outer + interpack + impack + other + pl, in this sequence as applicable for the Centralised Procedure. Only one file per language is required. 'Combined' means presented as one document.

* = When labelling documents are submitted as a single file, the type 'interpack' should be used

Appendix 2.4: Agency Codes and Names

The table below provides the list of Agencies as identified on the Heads of Medicines Agency website, i.e. http://www.hma.eu. The Agency Code is the value to use from within the EU Module 1 XML file.

Country	Agency Code	Human/Vet (H/V)	Agency Name
Austria	AT-AGES	H/V	Austria - BASG-Federal Office for Safety in Health Care (AGES-PharmMed LCM)
Belgium	BE-FAMHP	H/V	Belgium - Agence Fédérale des Médicaments et des Produits de Santé
Bulgaria	BG-BDA	H	Bulgaria - Bulgarian Drug Agency
	BG-NVS	V	Bulgaria - Institute for Control of Veterinary Product
Cyprus	CY-VS	H/V	Cyprus - Ministry of Health Pharmaceutical Services
Czech Rep.	CZ-SUKL	H	Czech Rep - State Institute for Drug Control
	CZ-USKVBL	V	Czech Rep - Institute for State Control of Veterinary Biologicals and Medicaments
Denmark	DK-DKMA	H/V	Denmark - Danish Medicines Agency
Estonia	EE-SAM	H/V	Estonia - State Agency of Medicines
EU	EU-EMEA	H/V	EMEA - European Medicines Agency
Finland	FI-NAM	H/V	Finland - National Agency for Medicines
France	FR-AFSSAPS	H	France - AFSSAPS - Agence Française de Sécurité Sanitaire des Produits de Santé
	FR-ANMV	V	France - ANMV - Agence Nationale du Médicament Vétérinaire, Agence Française de Sécurité Sanitaire des Aliments
Germany	DE-BFARM	H	Germany - BfArM - Bundesinstitut für Arzneimittel und Medizinprodukte
	DE-BVL	V	Germany – BVL - Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Ref. 301
	DE-PEI	H/V	Germany – PEI - Paul-Ehrlich Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel
Greece	EL-EOF	H/V	Greece - EOF - National Drug Organisation
Hungary	HU-IVMP	V	Hungary - Institute for Veterinary Medicinal Products
	HU-OGYI	H	Hungary - National Institute of Pharmacy
Iceland	IS-IMCA	H/V	Iceland - Icelandic Medicines Control Agency
Ireland	IE-IMB	H/V	Ireland - Irish Medicines Board
	IE-DAFF	V	Ireland - Dept of Agriculture & Food
Italy	IT-AIFA	H	Italy - Agenzia Italiana del Farmaco
	IT-LMV	V	Italy - Laboratorio di Medicina Veterinaria, Istituto Superiore di Sanità
	IT-SPV	H/V	Italy - Ministero della Salute, Direzione Generale della Sanità Pubblica Veterinaria
Latvia	LV-ZVA	H/V	Latvia - State Agency of Medicines
Liechtenstein	LI-LLV	H/V	Liechtenstein - Kontrollstelle für Arzneimittel beim Amt für Lebensmittelkontrolle und Veterinärwesen
Lithuania	LT-SMCA	H	Lithuania - State Medicines Control Agency

Country	Agency Code	Human/Vet (H/V)	Agency Name
	LT-VVPI	V	Lithuania - Lithuanian State Inspection on Veterinary Preparations
	LT-VMVT	V	Lithuania - State Food and Veterinary Service
Luxembourg	LU-MINSANT	H/V	Luxembourg - Direction de la Santé Villa Louvigny Division de la Pharmacie et des Medicaments
Malta	MT-MRU	V	Malta - Medicines Regulatory Unit
	MT-MEDAUTH	H	Malta - Medicines Authority Divizjoni Tas-Sahha Bezzjoni Ghar-Regolazzjoni Tal-Medicini
Netherlands	NL-MEB	H/V	Netherlands - College ter Beoordeling van Geneesmiddelen Medicines Evaluation Board
Norway	NO-NOMA	H/V	Norway - The Norwegian Medicines Agency
Poland	PL-URPL	H/V	Poland - Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Portugal	PT-DGV	H/V	Portugal - DGV - Direcção Geral de Veterinária, Divisão de Meios de Defesa da Saúde Animal
	PT-INFARMED	H/V	Portugal - INFARMED - Instituto Nacional da Farmácia e do Medicamento Parque da Saúde de Lisboa
Romania	RO-ANM	H/V	Romania - National Medicines Agency
Slovak Rep.	SK-SIDC	H	Slovak Rep - State Institute for Drug Control
	SK-USKVBL	V	Slovak Rep - Institute for State Control of Veterinary Biologicals and Medicaments Biovetská 34
Slovenia	SI-JAZMP	H/V	Slovenia - Agency for Medicinal Products and Medical Devices of the Republic of Slovenia
Spain	ES-AGEMED	H/V	Spain - Agencia Española de Medicamentos y Productos Sanitarios
Sweden	SE-MPA	H/V	Sweden - Medical Products Agency
United Kingdom	UK-MHRA	H	Medicines and Healthcare products Regulatory Agency
	UK-VMD	V	VMD - Veterinary Medicines Directorate

Note that only ‘human’ agency codes/names should be used in the context of an eCTD submission.

Appendix 3: Modularised DTD for EU Module 1

eu-regional.dtd

```
<!--
PUBLIC "-//EU//DTD eCTD EU Backbone 1.4//EN"
In the eCTD File Organisation: "util/dtd/eu-regional.dtd"

August 2009

Contributors:
  AFSSAPS (Aziz Diop)
  EMEA (Laurent Desqueper)
  MEB (C.A. van Belkum)

Meaning or value of the suffixes:
  ?  : element must appear 0 or 1 time
  *  : element must appear 0 or more time
  +  : element must appear 1 or more times
  <none>: element must appear once and only once
-->

<!-- General declarations, external modules references..... -->
<!ENTITY % countries
"(at|be|bg|common|cy|cz|de|dk|ee|el|es|emea|fi|fr|hu|ie|is|it|li|lt|lu|lv|mt|nl|no|pl|pt|ro|se|si|sk|uk)">
<!ENTITY % languages "(bg|cs|da|de|el|en|es|et|fi|fr|hu|is|it|lt|lv|mt|nl|no|pl|pt|ro|sk|sl|sv)">

<!ENTITY % leaf-node "(( leaf | node-extension )*)">

<!ENTITY % envelope-module SYSTEM "eu-envelope.mod" >
%envelope-module;

<!ENTITY % leaf-module SYSTEM "eu-leaf.mod" >
%leaf-module;

<!ELEMENT specific (
  %leaf-node;
)>
<!ATTLIST specific
  country %countries; #REQUIRED
>
<!ELEMENT pi-doc (
  %leaf-node;
)>
<!ATTLIST pi-doc
  xml:lang %languages; #REQUIRED
  type     (spc|annex2|outer|interpack|impack|other|pl|combined) #REQUIRED
  country  %countries;    #REQUIRED
>

<!-- Root element ..... -->
<!ELEMENT eu:eu-backbone (
  eu-envelope,
  m1-eu
)>
```

```
<!ATTLIST eu:eu-backbone
   xmlns:eu       CDATA #FIXED   "http://europa.eu.int"
   xmlns:xlink    CDATA #FIXED   "http://www.w3c.org/1999/xlink"
   xml:lang       CDATA #IMPLIED
   dtd-version    CDATA #FIXED   "1.4"
>

<!-- ..................................................................... -->
<!ELEMENT m1-eu (
   m1-0-cover,
   m1-2-form?,
   m1-3-pi?,
   m1-4-expert?,
   m1-5-specific?,
   m1-6-environrisk?,
   m1-7-orphan?,
   m1-8-pharmacovigilance?,
   m1-9-clinical-trials?,
   m1-10-paediatrics?,
   m1-responses?,
   m1-additional-data?
)>

<!-- ..................................................................... -->
<!ELEMENT m1-0-cover (
   specific+
)>

<!-- ..................................................................... -->
<!ELEMENT m1-2-form (
   specific+
)>

<!-- ..................................................................... -->
<!ELEMENT m1-3-pi (
   m1-3-1-spc-label-pl?,
   m1-3-1-pim?,
   m1-3-2-mockup?,
   m1-3-3-specimen?,
   m1-3-4-consultation?,
   m1-3-5-approved?,
   m1-3-6-braille?
)>

<!ELEMENT m1-3-1-spc-label-pl (
   pi-doc+
)>
<!ELEMENT m1-3-1-pim (
   leaf
)>
<!ELEMENT m1-3-2-mockup (
   specific+
)>
<!ELEMENT m1-3-3-specimen (
   specific+
)>
<!ELEMENT m1-3-4-consultation (
   specific+
)>
```

```
<!ELEMENT m1-3-5-approved (
  specific+
)>
<!ELEMENT m1-3-6-braille (
  %leaf-node;
)>

<!-- ..................................................................... -->
<!ELEMENT m1-4-expert (
  m1-4-1-quality?,
  m1-4-2-non-clinical?,
  m1-4-3-clinical?
)>

<!ELEMENT   m1-4-1-quality              %leaf-node;>
<!ELEMENT   m1-4-2-non-clinical         %leaf-node;>
<!ELEMENT   m1-4-3-clinical             %leaf-node;>

<!-- ..................................................................... -->
<!ELEMENT m1-5-specific (
   m1-5-1-bibliographic?,
   m1-5-2-generic-hybrid-bio-similar?,
   m1-5-3-data-market-exclusivity?,
   m1-5-4-exceptional-circumstances?,
   m1-5-5-conditional-ma?
)>

<!ELEMENT m1-5-1-bibliographic                      %leaf-node;>
<!ELEMENT m1-5-2-generic-hybrid-bio-similar         %leaf-node;>
<!ELEMENT m1-5-3-data-market-exclusivity            %leaf-node;>
<!ELEMENT m1-5-4-exceptional-circumstances          %leaf-node;>
<!ELEMENT m1-5-5-conditional-ma  %leaf-node;>

<!-- ..................................................................... -->
<!ELEMENT m1-6-environrisk (
  (m1-6-1-non-gmo | m1-6-2-gmo)?
)>
<!ELEMENT   m1-6-1-non-gmo          %leaf-node;>
<!ELEMENT   m1-6-2-gmo              %leaf-node;>

<!-- ..................................................................... -->
<!ELEMENT m1-7-orphan (
  m1-7-1-similarity?,
  m1-7-2-market-exclusivity?
)>
<!ELEMENT   m1-7-1-similarity                   %leaf-node;>
<!ELEMENT   m1-7-2-market-exclusivity           %leaf-node;>

<!-- ..................................................................... -->
<!ELEMENT m1-8-pharmacovigilance (
  m1-8-1-pharmacovigilance-system?,
  m1-8-2-risk-management-system?
)>
<!ELEMENT   m1-8-1-pharmacovigilance-system         %leaf-node;>
<!ELEMENT   m1-8-2-risk-management-system           %leaf-node;>

<!-- ..................................................................... -->
<!ELEMENT m1-9-clinical-trials   %leaf-node;>
```

```
<!-- ..................................................................... -->
<!ELEMENT m1-10-paediatrics %leaf-node;>

<!-- ..................................................................... -->
<!ELEMENT m1-responses (
  specific+
)>

<!-- ..................................................................... -->
<!ELEMENT m1-additional-data (
  specific+
)>
```

eu-envelope.mod

```
<!--
In the eCTD File Organisation: "util/dtd/eu-envelope.mod"

Version 1.4
August 2009

Contributors:
   AFSSAPS (Aziz Diop)
   EMEA (Laurent Desqueper)
   MEB (C.A. van Belkum)

-->

<!-- ..................................................................... -->
<!ELEMENT eu-envelope (
          envelope+
)>

<!ELEMENT envelope (
          submission,
          applicant,
          agency,
          procedure,
          invented-name+,
          inn*,
          sequence,
          related-sequence*,
          submission-description
)>

<!-- ..................................................................... -->
<!ELEMENT submission                ( number?, tracking )  >
<!ELEMENT tracking                  ( number+ )>
<!ELEMENT number                    ( #PCDATA )>
<!ELEMENT applicant                 ( #PCDATA )>
<!ELEMENT agency                    EMPTY>
<!ELEMENT procedure                 EMPTY  >
<!ELEMENT invented-name             ( #PCDATA )>
<!ELEMENT inn                       ( #PCDATA )>
<!ELEMENT sequence                  ( #PCDATA )>
<!ELEMENT related-sequence          ( #PCDATA )>
<!ELEMENT submission-description    ( #PCDATA )>

<!-- ..................................................................... -->
<!ATTLIST submission
 type ( initial-maa | var-type1a | var-type1b | var-type2 | var-nat | extension | psur | renewal |
supplemental-info | fum | specific-obligation | asmf | pmf | referral | annual-reassessment | usr | paed-
article-29 | paed-article-46 | article-58 | notification-61-3 | transfer-ma | corrigendum | lifting-
suspension | withdrawal | reformat) #REQUIRED
 mode ( single | grouping | worksharing ) #IMPLIED
>
```

```
<!-- ..... -->
<!ATTLIST agency
code ( AT-AGES | BE-FAMHP | BG-BDA | BG-NVS | CY-VS | CZ-SUKL | CZ-USKVBL | DE-BFARM |
DE-BVL | DE-PEI | DK-DKMA | EE-SAM | EL-EOF | ES-AGEMED | FI-NAM | FR-AFSSAPS | FR-
ANMV | HU-IVMP | HU-OGYI | IE-IMB | IE-DAFF | IS-IMCA | IT-AIFA | IT-LMV | IT-SPV | LI-LLV | LT-
SMCA | LT-VVPI | LT-VMVT | LU-MINSANT | LV-ZVA | MT-MRU | MT-MEDAUTH | NL-MEB | NO-
NOMA | PL-URPL | PT-DGV | PT-INFARMED | RO-ANM | SE-MPA | SI-JAZMP | SK-SIDC | SK-
USKVBL | UK-MHRA | UK-VMD | EU-EMEA ) #REQUIRED>

<!-- ..... -->
<!ATTLIST procedure
 type (
   centralised
 | national
 | mutual-recognition
 | decentralised
 ) #REQUIRED
>

<!-- ..... -->
<!ENTITY % env-countries
"(at|be|bg|cy|cz|de|dk|ee|el|emea|es|fi|fr|hu|ie|is|it|li|lt|lu|lv|mt|nl|no|pl|pt|ro|se|si|sk|uk)">

<!-- ..... -->
<!ATTLIST envelope country %env-countries; #REQUIRED >
<!ATTLIST related-sequence country %env-countries; #IMPLIED >

<!-- +++ -->
```

eu-leaf.mod

```
<!--
In the eCTD File Organisation: "util/dtd/eu-leaf.mod"

Version 1.4
August 2009

Contributors:
   AFSSAPS (Aziz Diop)
   EMEA (Laurent Desqueper)
   MEB (C.A. van Belkum)

This is based on ich-ectd-3-2.dtd;

If the ich-ectd.dtd is modularized, this one could be replaced.
Hence, one is certain that the common and EU leaf are the same.
-->

<!-- ========================================================== -->
<!ELEMENT node-extension (title, (leaf | node-extension)+)>
<!ATTLIST node-extension
          ID ID #IMPLIED
          xml:lang CDATA #IMPLIED
>
```

```
<!-- ============================================================= -->
<!ENTITY % show-list " (new | replace | embed | other | none) ">
<!ENTITY % actuate-list " (onLoad | onRequest | other | none) ">
<!ENTITY % operation-list " (new | append | replace | delete) ">
<!ENTITY % leaf-element " (title, link-text?) ">
<!ENTITY % leaf-att '
 ID                    ID                    #REQUIRED
 application-version   CDATA                 #IMPLIED
 version               CDATA                 #IMPLIED
 font-library          CDATA                 #IMPLIED
 operation             %operation-list;      #REQUIRED
 modified-file         CDATA                 #IMPLIED
 checksum              CDATA                 #REQUIRED
 checksum-type         CDATA                 #REQUIRED
 keywords              CDATA                 #IMPLIED
 xmlns:xlink           CDATA                 #FIXED    "http://www.w3c.org/1999/xlink"
 xlink:type            CDATA                 #FIXED    "simple"
 xlink:role            CDATA                 #IMPLIED
 xlink:href            CDATA                 #IMPLIED
 xlink:show            %show-list;           #IMPLIED
 xlink:actuate         %actuate-list;        #IMPLIED
 xml:lang              CDATA                 #IMPLIED
 '>

<!ELEMENT leaf %leaf-element;>
<!ATTLIST leaf
        %leaf-att;
>
<!ELEMENT title (#PCDATA)>
<!ELEMENT link-text (#PCDATA | xref)*>

<!ELEMENT xref EMPTY>
<!ATTLIST xref
        ID              ID              #REQUIRED
        xmlns:xlink     CDATA           #FIXED "http://www.w3c.org/1999/xlink"
        xlink:type      CDATA           #FIXED "simple"
        xlink:role      CDATA           #IMPLIED
        xlink:title     CDATA           #REQUIRED
        xlink:href      CDATA           #REQUIRED
        xlink:show      %show-list;     #IMPLIED
        xlink:actuate   %actuate-list;  #IMPLIED
>

<!-- +++ -->
```