EU Module 1 Specification

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0.95.1	EU Regulators, interested parties	EU Regulatory Authorities (members TIGes and NtA), EFPIA, Pharma, other interested parties
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1.1		
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Distribution

Version	Name	Organisation
0.4	http://esubmission.eudra.org	
0.7	http://esubmission.eudra.org	
0.8	http://esubmission.eudra.org	
0.91		
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	
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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/enterprise/pharmaceuticals/eudralex/homev2.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,
- 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.

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, RTF is deemed acceptable by Member States and the European Medicines Agency (EMEA) for narrative documents to be included in Module 1. XML, image and archive formats are also accepted on an ad hoc basis. Note that all PDF files included in an eCTD (irrespective of the module) should be v1.4, 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 always be provided in addition to the PDF versions. Guidance should be sought with the individual agency regarding the provision of MS Word and other requested documents.

Table 1 Acceptable file formats for Module 1

Document	File Format	Remark
Cover letter	XML*, PDF, RTF	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, RTF XML*, PDF, RTF XML*, PDF, RTF	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 necessary as the hard paper copy contains the legally binding signature.
Product Information: • Product information text** • Packaging mock-ups • Reference to specimens	 ZIP, TGZ, PDF, RTF PDF PDF	Labelling texts can be submitted in ZIP or TGZ format according to the PIM Data Exchange Standard. In that context, images can be transmitted in JPEG, GIF, PNG, TIF, SVG, or MathML and PIM information is exchanged in XML. If a higher resolution is necessary for the mock-ups, use JPEG, GIF, PNG or SVG on a case-by-case basis.
Other	PDF, RTF	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 (e.g. RTF). 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 individual national guidances 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.

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

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 4 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 given in Appendix 3 of this specification.

Note that files can be referred to across modules i.e. content files in Modules 2 to 5 (in the index.xml) can be referred to from the eu-regional.xml (Module 1) and vice versa.

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`" should be 'emea'; for all other procedures, it should be repeated for each Member State involved in the procedure. Note that the country value 'common' should only be used to identify files applicable to all countries, and that the value 'common' should not be used in the envelope.

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 a '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 Procedure). 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" and language subdirectories in Module 1.3.1 have the appropriate language identifier.
    - For MR, Decentralised and National Procedures, the documents for each country are placed in an appropriately named subdirectory. As noted elsewhere, "common" may be an acceptable directory to use for documents submitted to all of the countries receiving the submission. 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 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. 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.

File Naming Convention

File names have fixed and variable components. Components are separated by a hyphen. No hyphens or spaces should be used within each component.

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 without separation 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), it is suggested that the word 'point' is written in full i.e. ‘1point5mg’.

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-tablet10mgannotated.pdf
nongmo.pdf

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 (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. The agency acknowledges the proper receipt and the result of the validation process (technical [e.g. virus check, XML check, etc.] and content based) to the company, e.g. through a email connection

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/enterprise/pharmaceuticals/eudralex/homev2.htm

Appendix 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**
application		This is the number assigned to the application by the receiving agency. If known to the applicant prior to submission, it can be added, but is not mandatory as many agencies cannot provide this number prior to submission. For all subsequent submissions after the initial-maa, the number is known and must be included. This element can be repeated for multiple application numbers that apply within a Member State or EMEA, e.g. <application> <number>12345</number> <number>67890</number> </application>	N/A	**Mandatory**	**Unique**
number			**EU/1/00/150/001**	**Optional**	**Repeatable**
applicant		The name of the company submitting the eCTD.	**PharmaCompany**	**Mandatory**	**Unique**
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**
atc		The Anatomical Therapeutic Chemical classification of the medicinal product. This can be the assigned or proposed code. The top-level code should be used if this code is included in the envelope.	**L01CA01**	**Optional**	**Repeatable**

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
submission		Provides minimal administrative information associated with the submission.	N/A	**Mandatory**	**Unique**
	type	The type of submission material sent to the regulatory agency. The following are the valid values: ▪ `initial-maa` = Initial Marketing Authorisation Application ▪ `supplemental-info` = Supplemental Information (could include, for example, response to validation issues or response to questions) ▪ `fum` = Follow-Up Measure (includes post-approval commitments for national MAs) ▪ `specific-obligation` = Specific Obligation ▪ `var-type1a` = Variation Type IA ▪ `var-type1b` = Variation Type IB ▪ `var-type2` = Variation Type II ▪ `extension` = Extension ▪ `psur` = Periodic Safety Update Report (PSUR) ▪ `renewal` = Renewal (yearly or 5-yearly) ▪ `asmf` = Active Substance Master File ▪ `referral` = Referral under Article 29, 30, 31, 35 or 36 ▪ `annual-reassessment` = Annual Reassessment ▪ `usr` = Urgent Safety Restriction ▪ `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 during assessment or withdrawal of a marketing authorisation ▪ `paed-article-29` = Paediatric submission, Article 29 ▪ `var-nat` = National variation (e.g. national variation to apply for a pack size that is already registered within an existing MRP/DCP authorisation) ▪ `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 N.B Officially, Roman numerals are used for variations, e.g. Type IA, Type II – the elements must remain Arabic, however.	**initial-maa**	**Mandatory**	**Unique**
procedure		Defines the procedure in use with the submission	N/A	**Mandatory**	**Unique**

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
	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 a previous submission to which this submission relates e.g. the responses to questions to a particular variation.	**0001** see guidance below on use	**Optional**	**Repeatable**
submission-description		This element is used to describe the submission	**Initial Submission**	**Mandatory**	**Unique**

Example of the use of the Related Sequence

A 'regulatory activity' is a logical unit of submission activity (eg, 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.

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	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
0004	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
0005	Responses to questions on Type II variation for 'Treatment of Pain' indication	0003	This is a continuation of the regulatory activity initiated in 0003 and so the related sequence points to the beginning of that activity
0006	Responses to questions on Type II variation for change in manufacturing site (Westferry)	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	Line 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
0008	Updated, agreed, product information taking into account new indication ('Treatment of Pain')	0003	This is the completion of the new indication ('Treatment of Pain') activity
0009	Updated, agreed product information for the iv formulation	0007	This is the completion of the new dosage form (iv solution) activity

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	Destination code, usually referred to as country code as per Appendix 2.1
LL	Language code as per Appendix 2.2
EXT	File extension.
SPCDOC	Document identifier as per Appendix 2.3
VAR	Variable component of the filename.
DDDD	A sequence number made of 4 digits (e.g. 0000)
AR	Choice between “a” for applicant and “r” for regulator

* = 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. Note that the tracking table required with MPR/DCP submissions should be located within a 'common' directory, with the filename 'tracking.pdf' or 'tracking.xml’.
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. Additional documents should be included / attached with the Cover Letter in Section 1.0.

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 apply to all countries in MRP 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 hyphens or spaces. In the case of a Decentralised Procedure, the 'common' folder should be used.
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	SPC, Labelling and Package Leaflet
	Element	m1-3-1-spc-label-pl
	Directory	m1/eu/13-pi/131-spclabelpl
	Comment	General placeholder for SPC, 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	
	File	m1/eu/13-pi/131-spclabelpl/*CC*/*CC-SPCDOC-VAR.EXT*
	Comment	Case 1: there is only one language for the country Filename for the spc-label-pl document composed of a fixed component "*CC*", a fixed component "SPCDOC" as per table of Appendix 2.3 and an optional variable component to be used if needed. Example: m1/eu/13-pi/131-spclabelpl/fr/fr-spc-tablet10mgannotated.pdf.
13	Number	
	Title	
	Element	
	Directory	m1/eu/13-pi/131-spclabelpl/*CC*/*LL*
	Comment	Case 2: there are multiple languages for the country Always use a language directory at this level where files in multiple languages could be submitted to one country during the lifecycle of the submission. See Row 14 for an example.

14	Number	
	Title	
	Element	
	File	m1/eu/13-pi/131-spclabelpl/*CC*/*LL*/*CC*-*SPCDOC*-*VAR*.*EXT*
	Comment	Filename for the spc-label-pl document composed by a fixed component "*CC*", a fixed component "SPCDOC" 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).
15	Number	1.3.1
	Title	SPC, 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 is used when submitting Product Information in PIM format The name of the PIM submission is composed by a fixed component "131", a fixed component "pim", the 4-digit sequence of the PIM submission, and the fixed component AR (which can be "a" for applicant, or "r" for regulator). Example: m1/eu/13-pi/131-pim-0000-a.zip represents the first PIM submission of an applicant in ZIP format.
16	Number	1.3.2
	Title	Mock-up
	Element	m1-3-2-mockup
	Directory	m1/eu/13-pi/132-mockup
	Comment	
17	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.

18	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).
19	Number	1.3.3
	Title	Specimen
	Element	m1-3-3-specimen
	Directory	m1/eu/13-pi/133-specimen
	Comment	
20	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.
21	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).
22	Number	1.3.4
	Title	Consultation with Target Patient Groups
	Element	m1-3-4-consultation
	Directory	m1/eu/13-pi/134-consultation
	Comment	

23	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.
24	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).
25	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	
26	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.

27	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 (e.g. fr-approved-poland.pdf, fr-approved-manumber.pdf).
28	Number	1.3.6
	Title	Braille
	Element	m1-3-6-braille
	Directory	m1/eu/13-pi/136-braille
	Comment	
29	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).
30	Number	1.4
	Title	Information about the Experts
	Element	m1-4-expert
	Directory	m1/eu/14-expert
	Comment	General placeholder for Expert Information.
31	Number	1.4.1
	Title	Quality
	Element	m1-4-1-quality
	Directory	m1/eu/14-expert/141-quality
	Comment	General placeholder for quality information.

32	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).
33	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.
34	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).
35	Number	1.4.3
	Title	Clinical
	Element	m1-4-3-clinical
	Directory	m1/eu/14-expert/143-clinical
	Comment	General placeholder for clinical information.
36	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).

37	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.
38	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.
39	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).
40	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.
41	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).

42	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.
43	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).
44	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.
45	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).
46	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.

47	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).
48	Number	1.6
	Title	Environmental Risk Assessment
	Element	m1-6-environrisk
	Directory	m1/eu/16-environrisk
	Comment	General placeholder for Environmental Risk Assessment.
49	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.
50	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).
51	Number	1.6.2
	Title	GMO
	Element	m1-6-2-gmo
	Directory	m1/eu/16-environrisk/162-gmo
	Comment	General placeholder for GMO.

52	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).
53	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.
54	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.
55	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.
56	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.

57	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.
58	Number	1.8
	Title	Information relating to Pharmacovigilance
	Element	m1-8-pharmacovigilance
	Directory	m1/eu/18-pharmacovigilance
	Comment	General placeholder for information on pharmacovigilance.
59	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.
60	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.
61	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.

62	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.
63	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.
64	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.
65	Number	1.10
	Title	Information relating to Paediatrics
	Element	m1-10-paediatrics
	Directory	m1/eu/110-paediatrics
	Comment	General placeholder for information on paediatrics.
66	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.

67	Number	
	Title	Responses to Questions
	Element	m1-responses
	Directory	m1/eu/responses
	Comment	
68	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.
69	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).
70	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 applicable for the Centralised Procedure. The only occasion where this section should be used for all procedures is when an old version of a DTD is being used, during an agreed transition period, to support inclusion of a newly defined section of Notice to Applicants (refer to guidance issued with specification).

71	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.
72	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 'Additional Data' section should only be used for information required for National, MR and Decentralised Procedures; it is therefore not applicable for the Centralised Procedure.
73	Number	
	Title	
	Element	
	Directory	m1/eu/util
	Comment	Additional folder to hold utility files used in EU Region only.
74	Number	
	Title	
	Element	
	Directory	m1/eu/util/dtd
	Comment	Additional folder to hold DTD files used in EU Region only.

75	Number	
	Title	
	Element	
	Directory	util/dtd
	Comment	ICH specified location for eCTD DTD files.
76	Number	
	Title	
	Element	
	Directory	util/style
	Comment	ICH specified location for eCTD style-sheet files. 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 code usually called “country code” or “*CC*” in this specification.

Code	Destination	Comment
at	Austria	ISO-3166-1 code
be	Belgium	ISO-3166-1 code
bg	Bulgaria	ISO-3166-1 code
common	All countries	This code should be used in MRP to place documents that are applicable to all countries participating in the procedure This code should be used in the Decentralised Procedure
cy	Cyprus	ISO-3166-1 code
cz	Czech Republic	ISO-3166-1 code
de	Germany	ISO-3166-1 code
dk	Denmark	ISO-3166-1 code
ee	Estonia	ISO-3166-1 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 code
fi	Finland	ISO-3166-1 code
fr	France	ISO-3166-1 code
hu	Hungary	ISO-3166-1 code
ie	Ireland	ISO-3166-1 code
is	Iceland	ISO-3166-1 code
it	Italy	ISO-3166-1 code
li	Liechtenstein	ISO-3166-1 code
lt	Lithuania	ISO-3166-1 code
lu	Luxembourg	ISO-3166-1 code
lv	Latvia	ISO-3166-1 code
mt	Malta	ISO-3166-1 code
nl	Netherlands	ISO-3166-1 code
no	Norway	ISO-3166-1 code
pl	Poland	ISO-3166-1 code
pt	Portugal	ISO-3166-1 code
ro	Romania	ISO-3166-1-code
se	Sweden	ISO-3166-1 code
si	Slovenia	ISO-3166-1 code
sk	Slovakia	ISO-3166-1 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

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: SPC, Labelling and Package Leaflet File Name Identifiers

SPC 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	Text file with the concatenation of 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.

* = 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 - Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Ref. 301
	DE-PEI	H/V	Germany - Paul-Ehrlich Institut
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
	LT-VVPI	V	Lithuania - Lithuanian State Inspection on Veterinary Preparations

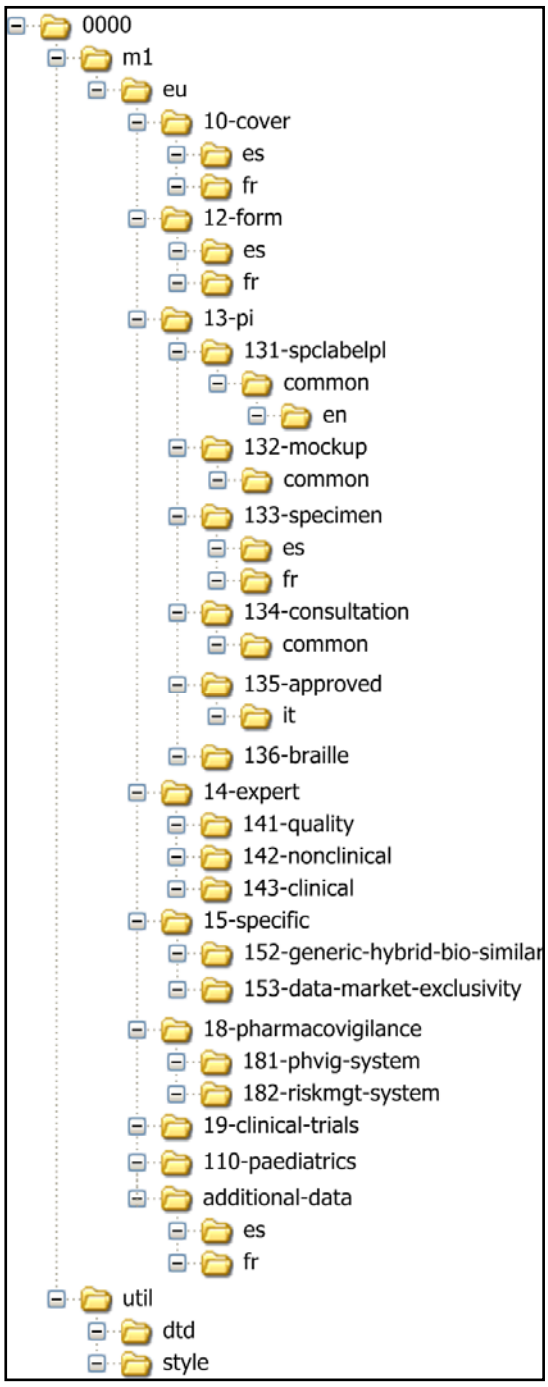
Country	Agency Code	Human/Vet (H/V)	Agency Name
	LT-VMVT	V	Lithuania - State Food and Veterinary Service
Luxembourg	LU-MINSANT	H/V	Luxembourg - Direction de la Santé Villa Louvigny Division de la Pharmacie et des Medicaments
Malta	MT-MRU	V	Malta - Medicines Regulatory Unit
	MT-MEDAUTH	H	Malta - Medicines 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 - Agencija za zdravila in medicinske pripmocke
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: Example Screenshots

This appendix is included to demonstrate how the directory structure may appear when applied to each procedure.

MRP Directory Structure



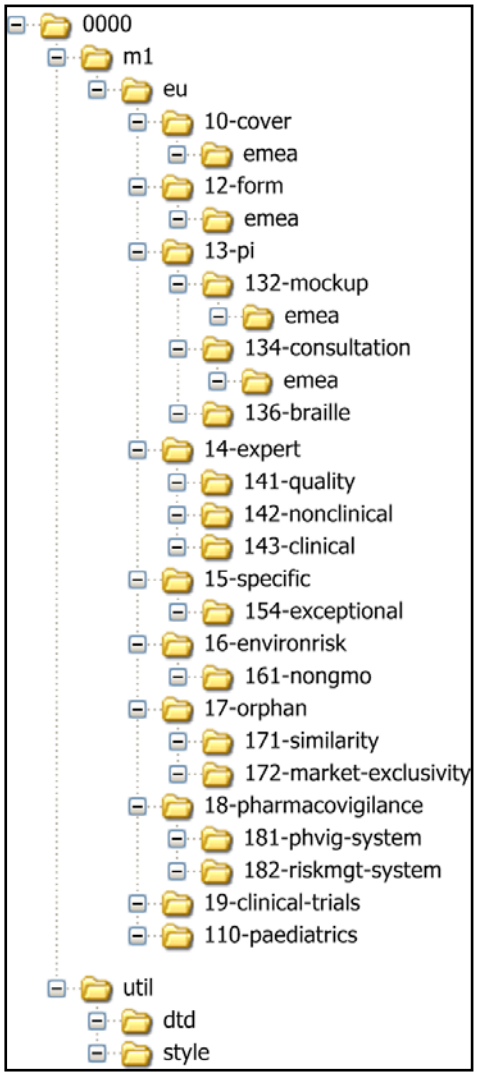
In the context of Mutual Recognition Procedure, 'common' is a directory used to hold files applicable to all countries involved in the procedure (cf. directory "132-mockup" in the example).

This example displays general use of the folder structure for all sections.

This example is provided with the following options:

- Italy as RMS,
- France and Spain as CMSs,
- submission of PI in PDF,
- generic, hybrid or bio-similar application

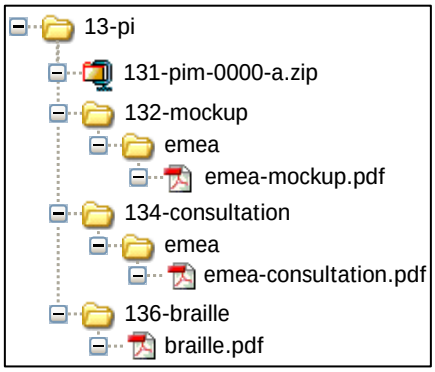
Centralised Procedure Directory Structure

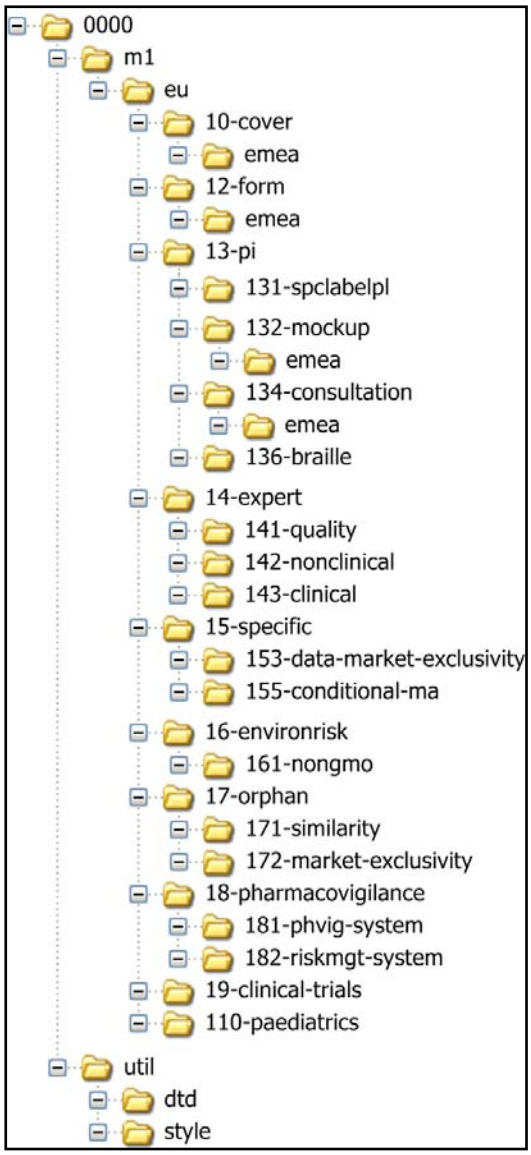


For the Centralised Procedure, most documents will be in English and valid for all European countries. Files should be placed in the country directories inside the 'emea' directory (for instance cf. directory "10-cover").

This first example shows the submission of PI using the PIM format (a file named "131-pim-0000-a.zip" is used for instance). PIM file is included within the folder "13-pi" but displays below Section "1.3.1 SPC, Labelling and Package Leaflet".

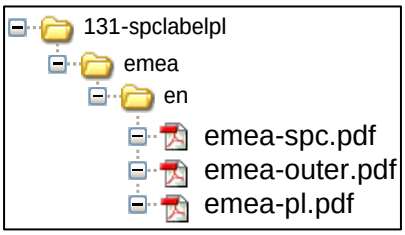
Section 1.3 is organised as follows in the context of the submission of product information in PIM format:



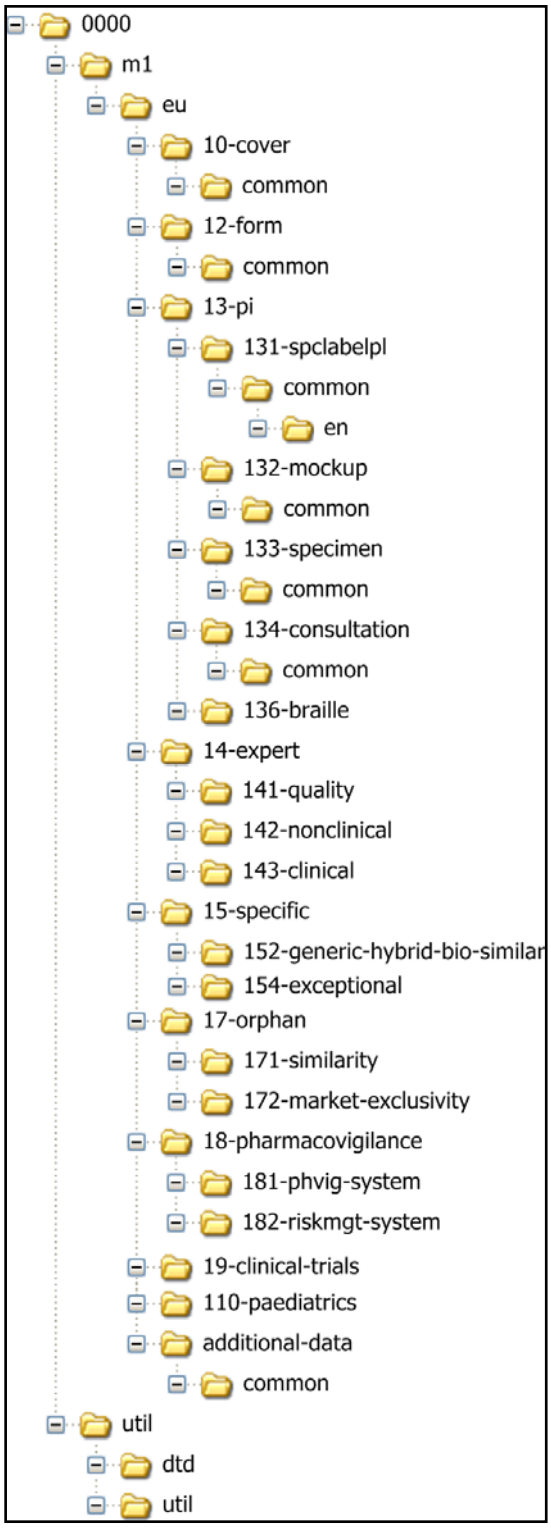


This second example shows the submission of PI using an electronic/paper-based format (e.g. PDF).

Section 1.3 is organised as follows in the context of the submission of product information in paper format (PDF):



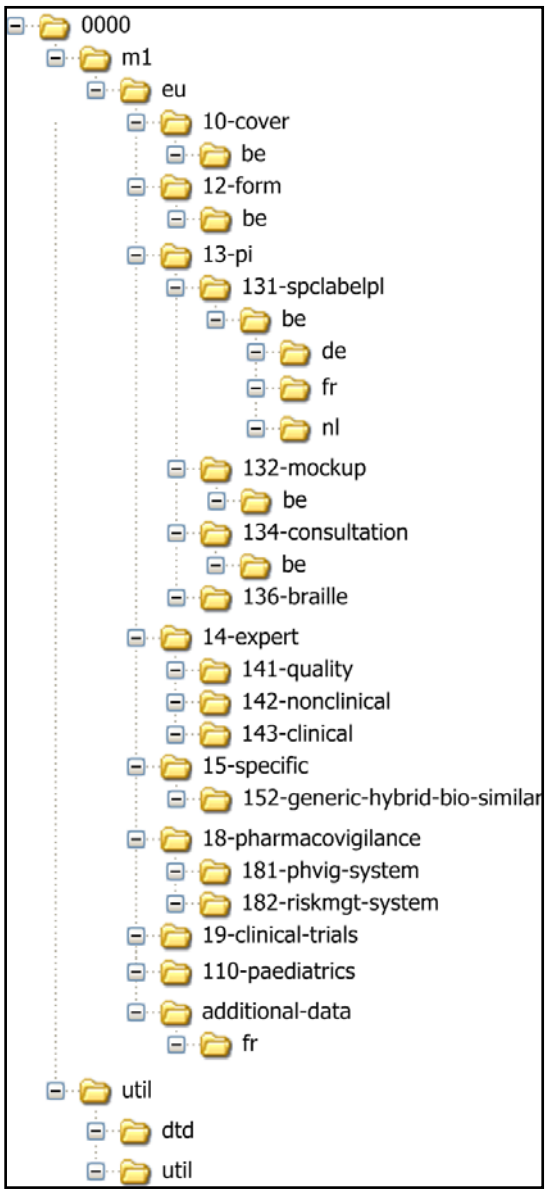
Decentralised Procedure Directory Structure



For the Decentralised Procedure, most documents will be in English and valid for all European countries.

Files should be placed in the common folder. No country or language folder should be added. Any national translations should be treated similar to a national submission (files to be located in country folder and optional language sub folder). At the end of the procedure the applicant needs to submit the national translations of the common approved SPC, Labelling and Package Leaflet. Similar to a national application, these documents should be located in the country specific folders and, if needed, in language specific sub-folders. For example: m1\eu\13-pi\131-spclabelpl\be\fr or m1\eu\13-pi\131-spclabelpl\be\nl.

National Procedure Directory Structure



This structure also allows files to be managed by language for a National Procedure.

Notes:

Section 1.3.3 ‘Specimen’ should contain files listing all of the physical specimens that are included with the submission, as the specimens are physical entities that cannot be submitted electronically.

Section 1.3.4 for all procedures has country sub-directories, as consultation is country-specific.

Appendix 4: Creating the XML EU Regional Submission

The name to be used as the directory name in the top-level directory is to be decided by the applicant, as the agency application number is not always known in advance and so cannot be used.

Furthermore, for the Mutual Recognition and Decentralised Procedures, the application number from one agency will be replaced by that of the receiving agency following submission as appropriate. The name given to the root directory is the decision of the applicant. However, the name must be a unique identifier for the application.

Details of the name used for the root directory should always be included in the cover letter. The new application and subsequent submissions in the form of supplemental information, variations, renewals, etc. should use the same top-level directory name. Each submission should be differentiated by a sub-directory named according to the sequence number of the submission to the EU regulatory agency. The agency application number (if available) and sequence number should be included in the "`eu-envelope`" element of the EU Regional instance. The first sub-directory below the top-level directory for the original submission should have the sequence number "0000" and e.g. the three subsequent submissions respectively "0001", "0002" and "0003".

The "`m1-eu`" element of the EU Regional XML instance is intended to provide information about and the location of individual files. Complete the following steps for all files being submitted for module 1.

1. Select a tag element that best corresponds to the document or file being submitted. For example, select the tag `<m1-0-cover>` to submit a file containing the cover letter for the submission.
   N.B. The operator used for the cover letter should always be "`new`".
   Create a child `<specific>` element for the `<m1-0-cover>` tag to identify for which country the cover letter is intended. The country information is stored in the attribute "`country`". When a file applies to all countries in the Centralised Procedure, it is recommended to use the "`emea`" country. In the case of Decentralised Procedure, it is recommended to use the "`common`" country.
2. Create a child `<leaf>` element for the `<specific>` tag created above. If more than one file belongs at this level (and country), you may create more than one `<leaf>` element under the tag.
3. Provide the relative location compared to the location of the `eu-regional.xml` file and file name of the actual file containing the cover letter using the "`xlink:href`" attribute for the `<leaf>` element (e.g. `xlink:href="10-cover/cover.pdf"`)
4. Provide a descriptive title for the file using the `<title>` element of the `<leaf>` element.
5. Provide information for the appropriate attributes of the `<leaf>` element as described in Appendix 2.

Where a section is not applicable, this section need not be included in the XML nor should a directory be created in the directory structure.

Instructions for a Simple New Submission

The following XML fragment demonstrates the submission of a cover letter, an application form and a SPC as part of a complete, new submission under the Centralised Procedure (i.e. only "emea" country appears).

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "../../util/dtd/eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="../../util/style/eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
       xmlns:xlink="http://www.w3c.org/1999/xlink"
       xml:lang="en" dtd-version="1.3">
   <eu-envelope>
      <envelope country="emea">
         <application>
            <number>APP-123456-EU</number>
         </application>
         <applicant>PharmaCompany</applicant>
         <agency code="EU-EMEA"/>
         <atc>L01CA01</atc>
         <submission type="initial-maa"/>
         <procedure type="centralised"/>
         <invented-name>WonderPill</invented-name>
         <inn>Pioglitazone hydrochloride</inn>
         <sequence>0000</sequence>
         <submission-description>A Simple Example</submission-description>
      </envelope>
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         <specific country="emea">
            <leaf  ID="cover-emea" operation="new" checksum-type="md5"
                   checksum="f066854eb3c5988235aa292bee43975a"
                   xlink:href="10-cover/emea/emea-cover.pdf">
               <title>Cover letter for Centralised Procedure</title>
            </leaf>
         </specific>
      </m1-0-cover>
      <m1-2-form>
         <specific country="emea">
            <leaf  ID="form-emea" operation="new" checksum-type="md5"
                   checksum="23aca8594462949cf24fa69398fe35a2"
                   xlink:href="12-form/emea/emea-form.pdf">
               <title>Application form for Centralised Procedure</title>
            </leaf>
         </specific>
      </m1-2-form>
      <m1-3-pi>
         <m1-3-1-spc-label-pl>
            <pi-doc type="spc" xml:lang="en" country="emea">
               <leaf  ID="spc" operation="new" checksum-type="md5"
                      checksum="9343456cd788e592321fea88590345f5"
                      xlink:href="13-pi/131-spclabelpl/emea/en/emea-spc.pdf">
                  <title>SPC in English</title>
               </leaf>
            </pi-doc>
         </m1-3-1-spc-label-pl>
      </m1-3-pi>
   </m1-eu>
</eu:eu-backbone>
```

Instructions for Submission of Supplemental Information

In this example, a new version of the SPC is submitted, e.g. as part of the answer of the company to the list of questions after the first round of assessment as included in a new cover letter.

To replace a file, add the replacement file `<leaf>` element under the same tag element as the original file.

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "../../util/dtd/eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="../../util/style/eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
       xmlns:xlink="http://www.w3c.org/1999/xlink"
       xml:lang="en" dtd-version="1.3">
   <eu-envelope>
      <envelope country="emea">
         <application>
            <number>APP-123456-EU</number>
         </application>
         <applicant>PharmaCompany</applicant>
         <agency code="EU-EMEA"/>
         <atc>L01CA01</atc>
         <submission type="supplemental-info"/>
         <procedure type="centralised"/>
         <invented-name>WonderPill</invented-name>
         <inn>Pioglitazone hydrochloride</inn>
         <sequence>0001</sequence>
         <related-sequence>0000</related-sequence>
         <submission-description>Response to Questions</submission-description>
      </envelope>
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         <specific country="emea">
            <leaf ID="cover-emea" operation="new" checksum-type="md5"
                  checksum="dd02956f9488ff802d37458d8a83e8e1"
                  xlink:href="10-cover/emea/emea-cover.pdf">
               <title>Cover letter for Centralised Procedure</title>
            </leaf>
         </specific>
      </m1-0-cover>
      <m1-3-pi>
         <m1-3-1-spc-label-pl>
            <pi-doc type="spc" xml:lang="en" country="emea">
               <leaf ID="spc" operation="replace" checksum-type="md5"
                     checksum="aa78949001e0d0cd00497564859d929f"
                     modified-file="../../../0000/m1/eu/eu-regional.xml#spc"
                     xlink:href="13-pi/131-spclabelpl/emea/en/emea-spc.pdf">
                  <title>SPC in English</title>
               </leaf>
            </pi-doc>
         </m1-3-1-spc-label-pl>
      </m1-3-pi>
   </m1-eu>
</eu:eu-backbone>
```

Instructions for MRP and DCP Submissions

This example depicts MRP or DCP submissions containing information for several agencies in order to highlight the use of the "common" country.

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "../../util/dtd/eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="../../util/style/eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
       xmlns:xlink="http://www.w3c.org/1999/xlink"
       xml:lang="en" dtd-version="1.3">
   <eu-envelope>
      <envelope country="es">
         <application>
            <number>APP-123456-MRP</number>
         </application>
         <applicant>PharmaCompany</applicant>
         <agency code="ES-AGEMED"/>
         <atc>L01CA01</atc>
         <submission type="initial-maa"/>
         <procedure type="mutual-recognition"/>
         <invented-name>WonderPill</invented-name>
         <inn>Pioglitazone hydrochloride</inn>
         <sequence>0000</sequence>
         <submission-description>Submission for Spain</submission-description>
      </envelope>
      <envelope country="fr">
         <application>
            <number>APP-123456-MRP</number>
         </application>
         <applicant>PharmaCompany</applicant>
         <agency code="FR-AFSSAPS"/>
         <atc>L01CA01</atc>
         <submission type="initial-maa"/>
         <procedure type="mutual-recognition"/>
         <invented-name>WonderPill</invented-name>
         <inn>Pioglitazone hydrochloride</inn>
         <sequence>0000</sequence>
         <submission-description>Submission for France</submission-description>
      </envelope>
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         <specific country="common">
            <leaf  ID="cover-common" operation="new" checksum-type="md5"
                   checksum="4c23c947735aa6e6f6934510f0c0e037"
                   xlink:href="10-cover/common/common-cover.pdf">
               <title>Cover letter</title>
            </leaf>
         </specific>
      </m1-0-cover>
      <m1-2-form>
         <specific country="common">
            <leaf  ID="form-common" operation="new" checksum-type="md5"
                   checksum="99cc390fe856736f620109aa0f0e034c"
                   xlink:href="12-form/common/common-form.pdf">
               <title>Application form</title>
            </leaf>
         </specific>
      </m1-2-form>
      <m1-3-pi>
         <m1-3-1-spc-label-pl>
            <pi-doc type="spc" xml:lang="en" country="common">
               <leaf  ID="spc-en" operation="new" checksum-type="md5"
```

```
                  checksum="111a988f8e88c734956fec92ca88a851"
                  xlink:href="13-pi/131-spclabelpl/common/en/common-spc.pdf">
                  <title>SPC in English</title>
               </leaf>
            </pi-doc>
         </m1-3-1-spc-label-pl>
      </m1-3-pi>
   </m1-eu>
</eu:eu-backbone>
```

Instructions to Migrate PI from Paper to PIM

Initial submissions may have been submitted including Product Information in paper (i.e. MS Word and PDF documents). When migrating to PIM, the Lifecycle Management operations must be used to:

- delete the previously PI submitted in paper (all formats)
- submit PIM as new

```
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "../../util/dtd/eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="../../util/style/eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
      xmlns:xlink="http://www.w3c.org/1999/xlink"
      xml:lang="en" dtd-version="1.3">
   <eu-envelope>
      …
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         …
      </m1-0-cover>
      <m1-2-form>
         …
      </m1-2-form>
      <m1-3-pi>
         <m1-3-1-spc-label-pl>
            <pi-doc type="spc" xml:lang="fr" country="fr">
               <leaf  ID="fr-doc" operation="delete"
                      modified-file="../../../0000/m1/eu/eu-regional.xml#fr-doc">
                  <title>SPC in French – MS Word</title>
               </leaf>
               <leaf  ID="fr-pdf" operation="delete"
                      modified-file="../../../0000/m1/eu/eu-regional.xml#fr-pdf">
                  <title>SPC in French - PDF</title>
               </leaf>
            </pi-doc>
            <pi-doc type="spc" xml:lang="nl" country="nl">
               <leaf  ID="nl-doc" operation="delete"
                      modified-file="../../../0000/m1/eu/eu-regional.xml#nl-doc">
                  <title>SPC in Dutch – MS Word</title>
               </leaf>
               <leaf  ID="nl-pdf" operation="delete"
                      modified-file="../../../0000/m1/eu/eu-regional.xml#nl-pdf">
                  <title>SPC in Dutch - PDF</title>
               </leaf>
            </pi-doc>
         </m1-3-1-spc-label-pl>
         <m1-3-1-pim>
            <leaf  ID="id-pim" operation="new" checksum-type="md5"
                   checksum="655eed921cb89904f732db021ca4ee15"
                   xlink:href="13-pi/131-pim-0001-a.zip">
               <title>PIM Submission 0001-a</title>
```

```
            </leaf>
          </m1-3-1-pim>
        </m1-3-pi>
    </m1-eu>
</eu:eu-backbone>
```

Appendix 5: Modularised DTD for EU Module 1

eu-regional.dtd

```
<!--
PUBLIC "-//EU//DTD eCTD EU Backbone 1.3//EN"
In the eCTD File Organisation: "util/dtd/eu-regional.dtd"

Version 1.3
May 2008

Contributors:
        AFSSAPS (Aziz Diop)
        EMEA (Laurent Desqueper, Carrasco Benitez)
        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|common|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)">

<!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
>
```

```
<!-- 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    "1.3 "
>

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

<!-- ..................................................................... -->
<!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 1.3
May 2008

Contributors:
          AFSSAPS (Aziz Diop)
          EMEA (Laurent Desqueper, Carrasco Benitez)
          MEB (C.A. van Belkum)
-->

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

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

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

<!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
>

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

eu-leaf.mod

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

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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
>
```