



EU Module 1 Specification

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Document Control

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1.2		
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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 (if required),
- information relating to orphan market exclusivity (if required),
- information relating to pharmacovigilance,
- information relating to clinical trials (if required).

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 kind of documents 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 (EMA) for narrative documents to be included in Module 1. XML, image and archive formats are also accepted on an ad hoc basis.

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 be provided inside the backbone and always 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

Document	File Format	Remark
Administrative forms: <ul style="list-style-type: none"> Application form and its annexes Variation application form incl. background for the variation Renewal form and its annexes 	XML, PDF, RTF PDF, RTF PDF, RTF	Documents should be generated from electronic source documents, any signature may be embedded as 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: <ul style="list-style-type: none"> Labelling 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

* = SPC, Package Leaflet, packaging texts

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 non-common formats (e.g. RTF) other than the common formats. However, the use of formats other than those specified by the ICH eCTD Specification Document is discouraged.

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.

Envelope

The `eu-envelope` element is designed to be used for all types of submissions (initial, supplemental, 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. Depending on the procedure for which the eCTD is intended (i.e. Centralised, Decentralised, MR or National Procedure), the `eu-envelope` may be a single envelope in the backbone containing multiple entries, one per country.

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 life cycle 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 Specifications provides directory and file structure that is strongly recommended:

- The same high-level directory structure is used for all 3 procedures (MR, National and Centralised Procedure). This is possible, despite the fact that files for MRP 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.
- For the Centralised Procedure, documents should be placed in language sub-directories for all languages within the ‘emea’ country directory.
- For MRP and National Procedures, language sub-directories should only be used in the appropriate country directories where necessary, for example when documents in more than one language are submitted to a country (e.g. Belgium).

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 mandatory. 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 must 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 must be the document type code as per Appendix 2 and 2.3. The third component if necessary should be the variable component.

There are no recommendations for variable components in this specification. The format of the file is indicated by the file extension. File names must always be in lowercase.

Examples:

```
fr-cover.pdf
de-cover-response.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 the 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 at least by 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 secure 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 would send it to the applicant e.g. through a secure 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 can be country specific	N/A	Mandatory	Unique
envelope		Parent element for the submission meta-data. This element can be country-specific.	N/A	Mandatory	Repeatable
	country	The country to which the envelope applies. If the envelope applies to all countries, country “emea” should be used	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 preceding 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 for different Member States 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-name		The name of the receiving agency	EMEA	Mandatory	Repeatable
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	<p>The type of submission material sent to the regulatory agency. The following are the valid values:</p> <ul style="list-style-type: none"> ▪ initial-maa = Initial marketing authorisation application ▪ supplemental-info = Supplemental information after questions ▪ follow-up = Follow-up measure ▪ specific-obligation = Specific obligation ▪ var-type1a = Variation type 1a ▪ var-type1b = Variation type 1b ▪ var-type2 = Variation type 2 ▪ psur = Periodic Safety Update Report ▪ renewal = Renewal ▪ dmf = Drug master file ▪ arbitration = Arbitration under article 29, 30 or 31 ▪ cond-specific-obligation = Specific obligation following conditional approval ▪ safety = Safety restriction <p>N.B Officially, the Roman numerals are used for variations, e.g. Type Ia, Type II – the elements must remain Arabic, however.</p>	initial-maa	Mandatory	Unique
procedure		Defines the procedure in use with the submission	N/A	Mandatory	Unique
	type	<p>The type of procedure for the submission. The following are the valid values:</p> <ul style="list-style-type: none"> ▪ 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

Element	Attribute	Description/Instructions	Example	Constraint	Occurrence
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
	country	This optional element is provided for potential use under the MRP procedure, if necessary.	emea	Optional	Unique
submission-description		This element is used to describe the submission	Initial Submission	Mandatory	Unique

Example of the use of the Related Sequence

When providing supplemental information to an original application or a variation, you should include the sequence number of the earlier submission in the related-sequence element. If this submission is related to more than one previous submission, you should provide each previous submission's sequence number in a separate related-sequence-number element. There is no limit to the number of related-sequence-number elements. The following is an example of the related sequence number. An application has the following submissions:

Submission	Sequence	Related Sequence
0000 - Original MAA application	0000	<none>
0001 - Responses to questions on the original application	0001	0000
0002 - Responses to further questions on the original application	0002	0000
0003 - A technical variation	0003	<none>
0004 - A labelling change variation	0004	<none>
0005 - Responses to questions on the technical variation	0005	0003
0006 - Responses to questions on the labelling change variation	0006	0004
0007 - A new dosage form variation that amends information provided in the original application and the technical variation	0007	<none>

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
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 life cycle 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, fr-cover-response.pdf). When only the cover letter is submitted in this directory the file name should be CC-cover.pdf. Additional documents such as rationale for variation, response to questions, etc 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 life cycle 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 more than one country 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 life cycle 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 E.g. m1/eu/13-pi/131-spc-label-pl/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 life cycle of the submission.

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/be/nl/be-spc-tablet10mgannotated.pdf, m1/eu/13-pi/131-spclabelpl/emea/de/emea-combined-tablet10mggerman.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 life cycle 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 life cycle 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 life cycle 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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	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- <i>VAR.EXT</i>
	Comment	Filename for the information on similarity composed by a fixed component “similarity” and an optional variable component to be used if needed (e.g. similarity.pdf).
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- <i>VAR.EXT</i>
	Comment	Filename for information on market exclusivity composed by a fixed component "marketexclusivity" and an optional variable component to be used if needed (e.g. marketexclusivity.pdf).
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- <i>VAR.EXT</i>
	Comment	Filename for information on pharmacovigilance system composed by a fixed component "phvigsystem" and an optional variable component to be used if needed (e.g. phvigsystem.pdf).
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- <i>VAR.EXT</i>
	Comment	Filename for information on pharmacovigilance system composed by a fixed component "riskmgtsystem" and an optional variable component to be used if needed (e.g. riskmgtsystem.pdf).
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- <i>VAR.EXT</i>
	Comment	Filename for information on clinical trials composed by a fixed component "clinicaltrials" and an optional variable component to be used if needed (e.g. clinicaltrials.pdf).
65	Number	
	Title	Responses to Questions
	Element	m1-responses
	Directory	m1/eu/responses
	Comment	
66	Number	
	Title	
	Element	
	Directory	m1/eu/responses/ <i>CC</i>
	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 life cycle of the submission.

67	Number	
	Title	
	Element	
	File	<i>m1/eu/responses/CC/CC-responses-VAR.EXT</i>
	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).
68	Number	
	Title	Additional Data
	Element	m1-additional-data
	Directory	m1/eu/additional-data
	Comment	
69	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 life cycle of the submission.
70	Number	
	Title	
	Element	
	File	<i>m1/eu/additional-data/CC/CC-additionaldata-VAR.EXT</i>
	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).
71	Number	
	Title	
	Element	
	Directory	m1/eu/util
	Comment	Additional folder to hold utility files used in EU Region only.

72	Number	
	Title	
	Element	
	Directory	m1/eu/util/dtd
	Comment	Additional folder to hold DTD files used in EU Region only.
73	Number	
	Title	
	Element	
	Directory	util/dtd
	Comment	ICH specified location for eCTD DTD files
74	Number	
	Title	
	Element	
	Directory	util/style
	Comment	ICH specified location for eCTD Style-sheet files

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	Several Countries	This code should be used in MRP to place documents that correspond to more than one country 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

(*) Bulgaria and Romania countries are already supported in the EU Module 1 but these countries cannot be used before the formal accession date of these countries to the EU.

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

(*) Bulgarian and Romanian languages are already supported in the EU Module 1. This means that these languages are active in the EU Module 1 DTD. However, these languages should not be used before the formal accession date of Bulgaria and Romania to the EU. Refer to guidance to know when these languages can be effectively used in real submissions.

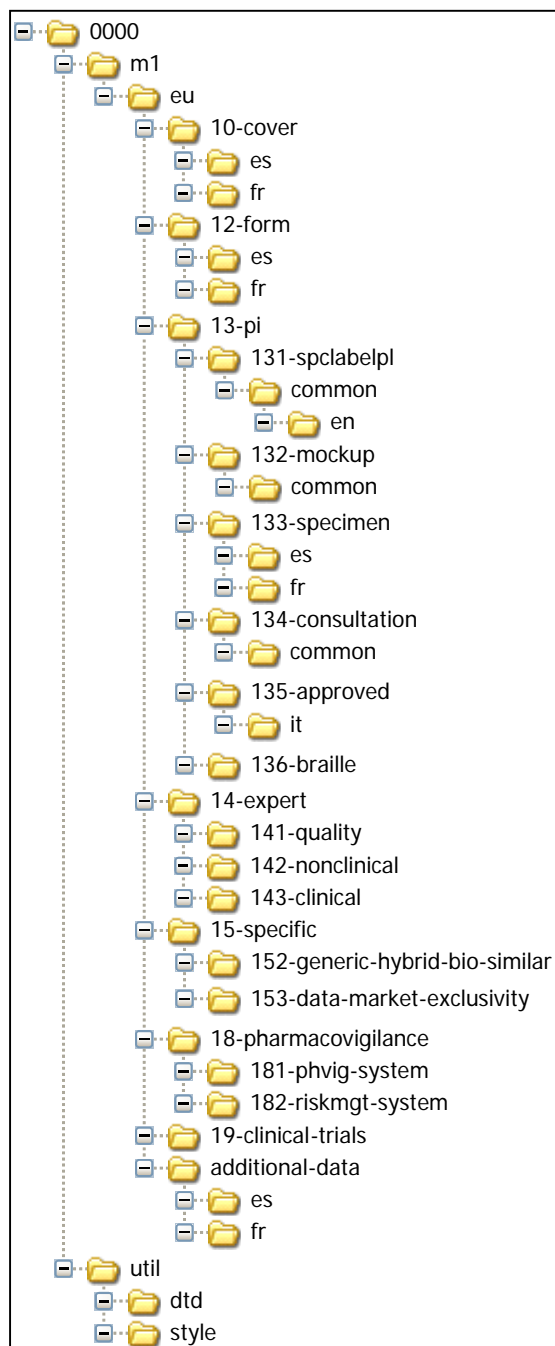
Appendix 2.3: SPC, Labelling and Package Leaflet File Name Identifiers

SPC DOC	Description
spc	Summary of Product Characteristics
annex2	Annex II
outer	Outer Packaging
interpack	Intermediate Packaging
impack	Immediate Packaging
pl	Package Leaflet
other	Other product information
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.

Appendix 3: Example Screenshots

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

MRP Directory Structure



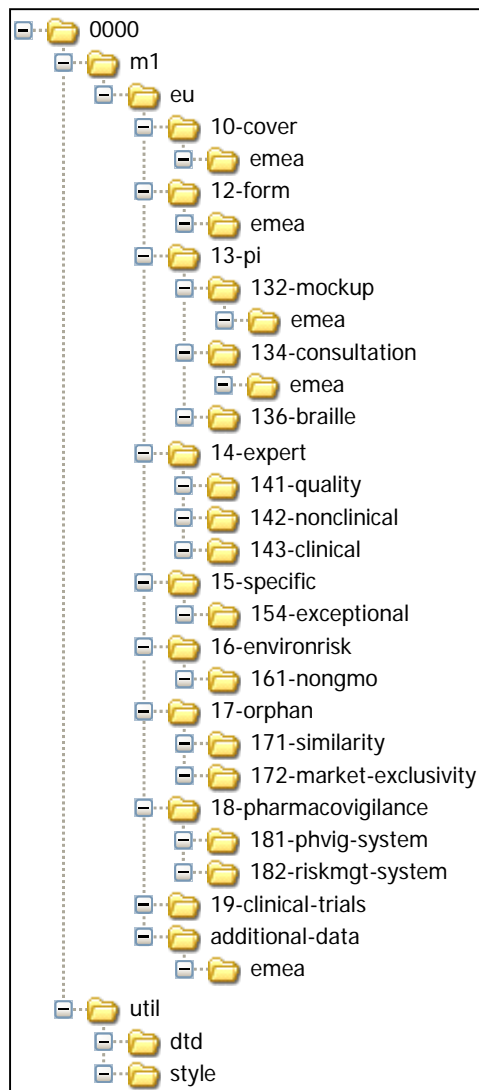
In the context of Mutual Recognition Procedure, 'common' is a directory used to hold files applicable to more than one country, or all countries involved in the procedure (cf. directory "132-mockup" in the example).

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

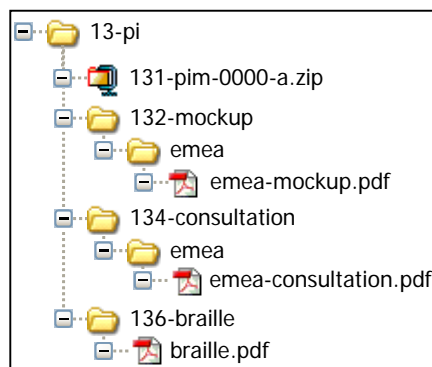
Centralised Procedure Directory Structure

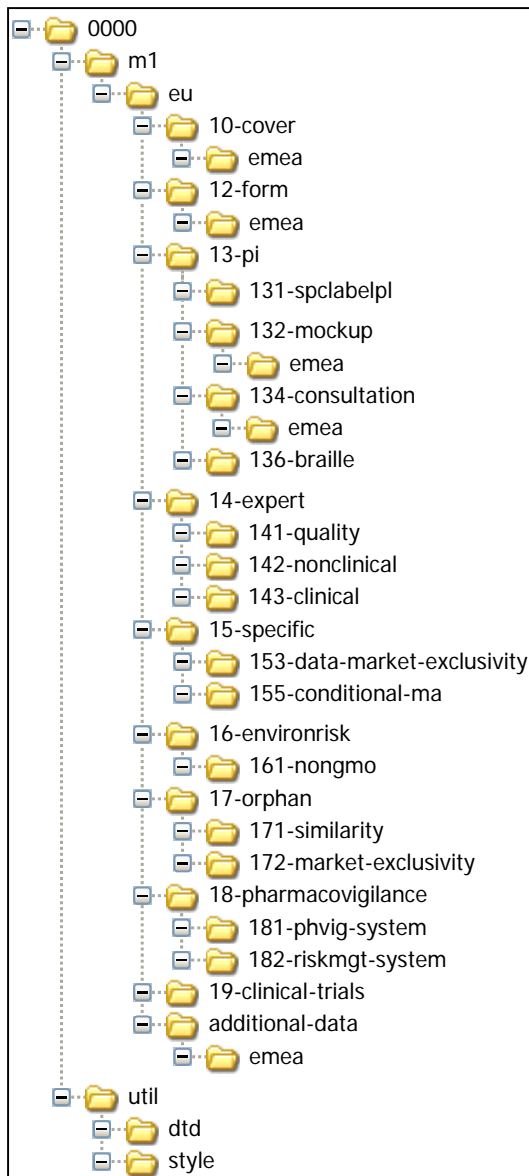


For the Centralised Procedure, most documents will be in English and valid for all European countries. Files should be placed in the country directories inside the 'emea' directory (for instance cf. directory "10-cover").

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".

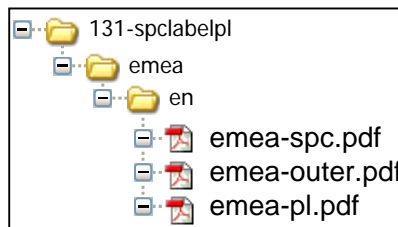
The section 1.3 is organised as follows in the context of the submission of product information in PIM format:



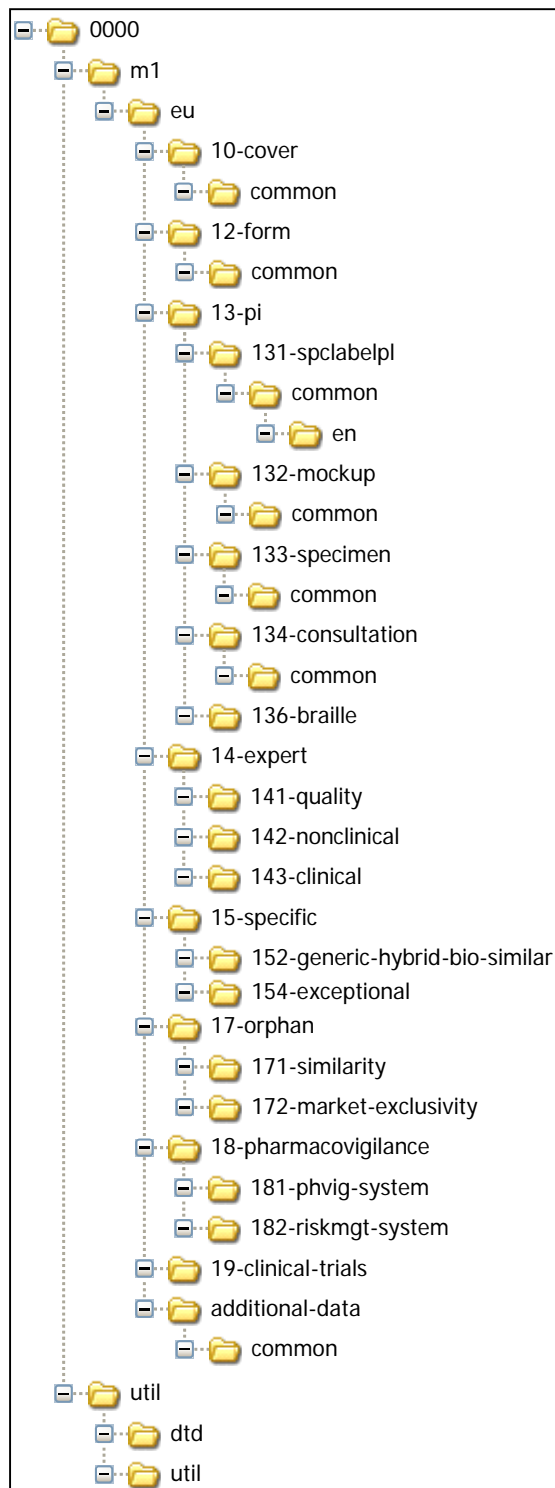


This second example shows the submission of PI using the paper format (e.g. PDF).

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



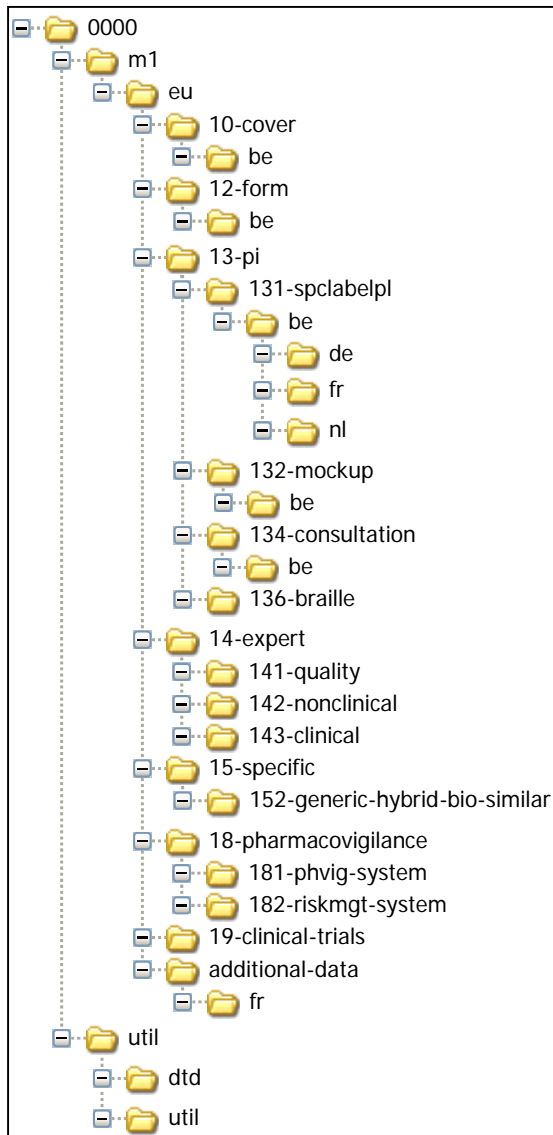
Decentralised Procedure Directory Structure



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-splabelpl\be\fr or m1\eu\13-pi\131-splabelpl\be\nl.

National Procedure Directory Structure



This structure also allows files to be managed by language for 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 Centralised Procedure (i.e. only "emea" country appears). This applies also to the Decentralised Procedure, expect the use of the "common" country instead of the "emea" 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="1.2.1">
  <eu-envelope>
    <envelope country="emea">
      <application>
        <number>APP-123456-EU</number>
      </application>
      <applicant>PharmaCompany</applicant>
      <agency-name>EMA</agency-name>
      <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="huhhchc3880cjp0dip0d0jo20ddoowckljj"
          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="huhhchc3880cjp0dip0d0jo20ddoowckljj"
          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="huhhchc3880cjp0dip0d0jo20ddoowckljj"
            xlink:href="13-pi/131-spc-label-pl/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="1.2.1">
  <eu-envelope>
    <envelope country="emea">
      <application>
        <number>APP-123456-EU</number>
      </application>
      <applicant>PharmaCompany</applicant>
      <agency-name>EMA</agency-name>
      <atc>L01CA01</atc>
      <submission type="initial-maa"/>
      <procedure type="centralised"/>
      <invented-name>WonderPill</invented-name>
      <inn>Pioglitazone hydrochloride</inn>
      <sequence>0001</sequence>
      <related-sequence>0000</related-sequence>
      <submission-description>Delta Submission</submission-description>
    </envelope>
  </eu-envelope>
  <m1-eu>
    <m1-0-cover>
      <specific country="emea">
        <leaf ID="cover-emea" operation="new" checksum-type="md5"
          checksum="huhhchc3880cjp0dip0d0jo20ddoowcklj"
          xlink:href="10-cover/emea/emea-cover.pdf">
          <title>Cover letter for Central 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="huhhchc3880cjp0dip0d0jo20ddoowcklj"
            modified-file="../0000/m1/eu/eu-regional.xml#spc"
            xlink:href="13-pi/131-spc-label-pl/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="1.2.1">
  <eu-envelope>
    <envelope country="common">
      <application>
        <number>APP-123456-MRP</number>
      </application>
      <applicant>PharmaCompany</applicant>
      <agency-name>Spanish Agency</agency-name>
      <agency-name>French Agency</agency-name>
      <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 Belgium</submission-description>
    </envelope>
  </eu-envelope>
  <m1-eu>
    <m1-0-cover>
      <specific country="common">
        <leaf ID="cover-common" operation="new" checksum-type="md5"
          checksum="huhhchc3880cjp0dip0d0jo20ddoowckljj"
          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="huhhchc3880cjp0dip0d0jo20ddoowckljj"
          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="huhhchc3880cjp0dip0d0jo20ddoowckljj"
            xlink:href="13-pi/131-spc-label-pl/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 Life Cycle 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="1.2.1">
  <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" checksum-type="md5"
            checksum="huhhchc3880cjp0dip0d0jo20ddoowckljj"
            modified-file="../.../0000/m1/eu/eu-regional.xml#fr-doc">
            <title>SPC in French - MS Word</title>
          </leaf>
          <leaf ID="fr-pdf" operation="delete" checksum-type="md5"
            checksum="huhhchc3880cjp0dip0d0jo20ddoowckljj"
            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" checksum-type="md5"
            checksum="huhhchc3880cjp0dip0d0jo20ddoowckljj"
            modified-file="../.../0000/m1/eu/eu-regional.xml#nl-doc">
            <title>SPC in Dutch - MS Word</title>
          </leaf>
          <leaf ID="nl-pdf" operation="delete" checksum-type="md5"
            checksum="huhhchc3880cjp0dip0d0jo20ddoowckljj"
            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 1.2.1//EN"  
In the eCTD File Organisation: "util/dtd/eu-regional.dtd"
```

```
Version 1.2.1  
October 2006
```

```
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|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
```

```
>
```

```

<!-- 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   "1.2.1"
>

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

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

```

eu-envelope.mod

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

Version 1.2.1
October 2006

Contributors:

AFSSAPS (Aziz Diop)
EMA (Laurent Desqueper, Carrasco Benitez)
MEB (C.A. van Belkum)

-->

<!-- -->

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

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

<!-- -->

```
<!ELEMENT application      ( number* )>  
<!ELEMENT applicant        ( #PCDATA )>  
<!ELEMENT agency-name      ( #PCDATA )>  
<!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 procedure  
  type (  
    centralised  
    | national  
    | mutual-recognition  
    | decentralised  
  ) #REQUIRED  
>
```

<!-- -->

```
<!ATTLIST submission
  type (
    initial-maa
    | supplemental-info
    | follow-up
    | specific-obligation
    | var-type1a
    | var-type1b
    | var-type2
    | psur
    | renewal
    | dmf
    | arbitration
    | cond-specific-obligation
    | safety
  ) #REQUIRED
>
```

```
<!-- ..... -->
<!ENTITY % countries
"(at|be|bg|common|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 %countries; #REQUIRED >
<!ATTLIST related-sequence country %countries; #IMPLIED >
```

eu-leaf.mod

<!--

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

Version 1.2.1

October 2006

Contributors:

AFSSAPS (Aziz Diop)

EMA (Laurent Desqueper, Carrasco Benitez)

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 | |

>