EU Module 1 Specification

draft version 0. 72

April, 2002

Status

This document is a draft. It is inappropriate to use it as reference material or to cite it other than as *work in progress*.

Introduction

This document specifies Module 1 of the electronic Common Technical Document (eCTD) for the European Union ("EU"). The latest version of this specification can be found at: http://esubmission.eudra.org/ectd/module1.

This document should be read together with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) eCTD Specification to prepare a valid eCTD submission in the EU. The current version of the ICH eCTD Specification can be found at: http://esubmission.eudra.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*: http://pharmacos.eudra.org/F2/eudralex/vol-2/home.htm.

In general the following type of information could be included in the first submission of an application for marketing authorisation of a medicinal product: application forms, product information documents, information on Experts, specific requirements for the application (*optional*) and the Environmental Risk Assessment (*optional*). Besides the documentation described by the Notice to Applicants other documents could be part of Module 1, e.g. cover letters, letters of authorisation, GMP certificates, etc.

It should be noted that for subsequent submissions in the lifecycle of a particular medicinal product, e.g. for a variation, not all of the above mentioned documents need be included in Module 1.

This document describes only the region specific information that is common to all submissions in the EU. Guidance on country specific information in Module 1 should be provided by the Member States. The directory structure as given in table 4 on page 6 includes country specific folders. 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. Conform the ICH eCTD Specification Document, these are the file formats that are deemed acceptable by Member States and the European Agency for the Evaluation of Medicinal Products (EMEA) for the documents in Module 1.

In line with the general principles of the eCTD, it is intended that XML will become the submission format for application forms and product information as they contain structured data. As the XML documents become available for practical implementation, they will be introduced into Module 1 and the current file formats will be replaced after a transition period.

Although the use of the file formats defined in table 1 is strongly recommended, individual Member States could still indicate a preference for other file formats in the country specific placeholder e.g. XML for application forms or product information documents.

Table 1

Document	File format	Remark
Administrative forms, i.e.: • Part 1a • Variation application form • Renewal form	 PDF, RTF PDF, RTF PDF, RTF	Documents should be generated from electronic source documents, any signature could be embedded as graphic file in the PDF text
Product Information: • SPC • PIL • Blister packaging • Outer packaging = Mock-up • Immediate packaging	 PDF, RTF PDF, RTF PDF, RTF PDF PDF, RTF	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

Modules 2 to 5.

No additional file formats are defined for Modules 2 to 5 other then those mentioned in the ICH eCTD Specification Document, Appendix 2. In line with the statement on regional use of other formats in that appendix of the ICH eCTD Specification, individual Member States could agree on a case-by-case basis with pharmaceutical companies to accept formats (e.g. RTF) other than the common formats.

General architectural approach to 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. The backbone must be a valid XML document according tot the XML EU Index Document Type Definition (DTD). The XML EU Index instance contains meta-data for the leaves, including pointers to the files in the directory structure. In addition, the XML EU Index DTD defines meta-data at the submission level in the form of an envelope. The root element is "eu-backbone" and contains two elements: "envelope" and "m1-eu". A full description of the EU Index DTD can be found in annex A to this guideline.

Envelope

The "envelope" element is designed to be used for all types of submissions for a given medicinal product (original, subsequent, variations, renewals, etc.) 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 Table 2 on page 5. Some elements included in the envelope are also part of the data model of the EuroPHARM database[1].

M-1-eu

The "m1-eu" element of the XML EU Index DTD is based on the same conceptual approach as the common part of the XML eCTD DTD. It provides a XML catalogue with meta-data at the leaf level including pointers to the location of files in a directory structure. This directory structure of Module 1 is reflected in the Template as provided by ICH with the additional structure as provided by the EU (see: http://esubmission.eudra.org/ectd/template). A tabular overview of this structure, including element names and titles is provided in table 3 on page 6. As for the XML eCTD DTD, the "m1-eu" element maps to the directory structure.

The "m1-eu" element is composed of six child-elements: application forms, product information, information on the Experts, specific requirements, annex (environmental risk assessment) and other. The attributes of the leaf element are identical to the leaf element attributes of the ICH eCTD DTD, see table 4 on page 11.

[1] A database in the design stage to contain relevant information on all authorised medicinal product on the European market.

EU approach to the product information part of Module 1

With respect to product information (PI) documents, the currently acceptable file formats are indicated in table 1 on page 3. In the near future, the EU will move into the direction of an XML approach for the exchange of product information taking into consideration the results of the Product Information Management (PIM) project. For additional details on the PIM project, see:
http://esubmission.eudra.org/pim.

EU approach to application forms in Module 1

Currently, the relevant administrative forms should be provided as files in a format as specified in table 1 on page 3. However, it is the intention of the EU to develop DTDs with associated style sheets for each of those individual forms, which will make automated processing possible. The administrative information in Module 1 will be normalised between those forms, the "envelope" and product information.

Table 2: Envelope Element Description

Element	Attribute	Description/Instructions	Example
envelope		Parent element for applicant, agency, agency-number, approval-date, product-name and submission	N/A
applicant*		The name of the company submitting the eCTD	**Super Pil Inc.**
agency		The name of the receiving agency	**EMEA**
agency-number*		The agency number linked to the application for the medicinal product.	**EMEA/H/134/II/04**
approval-date*		The date the product was approved, if known. Use the format "YYYY-MM-DD".	N/A
product-name*		The name of the medicinal product.	**Wonder Pil**
submission		Provides administrative information associated with the submission.	N/A
	type	The type of submission material sent to the regulatory agency. The following are the valid values: `presub` = Pre-submission `new` = New application `sup` = Supplemental information after questions `type1` = Variation type 1 `type2` = Variation type 2 `psur` = PSUR `renewal` = Renewal `dmf` = Drug master file	**new**
	submission-date	The date the `index.xml` and `eu-index.xml` files were submitted to the agency. Use the format "YYYY-MM-DD".	**2001-11-01**
	sequence-number	A unique sequence number assigned to each submission. Use "0000" for the new application and then increment by 1 for each subsequent submission.	**0000**

* = element with an asterisk will be a data-field in the EuroPharm database; the exact names of the data-fields are still under consideration; the information of the envelope could be imported in national databases and after a marketing authorisation, relevant elements could be exported via the national database to the EuroPharm database.

Table 3. File Organization for Module 1.

1	Number	1
	Title	Module 1 EU
	Element	m1-eu
	Directory	module-1/eu
	Comment	Top level directory for the EU
2	Number	
	Title	
	Element	
	File	module-1/eu/eu-index.xml
	Comment	The EU Index XML instance including the envelope
3	Number	
	Title	
	Element	
	File	module-1/eu/eu-index-checksum.txt
	Comment	The checksum of the EU Index XML instance
4	Number	1.0
	Title	Module 1 Member State specific part
	Element	m1-eu-country
	Directory	module-1/eu/country
	Comment	Where country is a two character code from ISO-3166-1.Placeholder for specific information e.g. on business process, file format, etc. per Member State. For example for France: m1-eu-fr and module-1/eu/fr.
5	Number	1.1
	Title	Module 1 EU common part
	Element	m1-eu-common
	Directory	module-1/eu/common
	Comment	Common part of Module 1 for the EU; documents that do not fit into one of the lower subcategory tags m1-2 to m1-6 should be placed under m1-7-other
6	Number	1.2
	Title	Application form
	Element	m1-2-application
	Directory	module-1/eu/common/application
	Comment	Either no or one of the following forms should be submitted in this folder: Part 1A, Variation Application Form or Renewal Form
7	Number	1.2.1
	Title	Part 1 A Form
	Element	m1-2-1-part1a
	File	module-1/eu/common/application/part1a.pdf
	Comment	
8	Number	1.2.2
	Title	Variation application form
	Element	m1-2-2-variation
	File	module-1/eu/common/application/variation.pdf
	Comment	Application form for both type 1 and type 2 variations

9	Number	1.2.3
	Title	Renewal form
	Element	m1-2-3-renewal
	File	module-1/eu/common/application/renewal.pdf
	Comment	
10	Number	1.3
	Title	Product Information
	Element	m1-3-pi
	Directory	data/module-1/eu/common/pi
	Comment	General placeholder for Product Information
11	Number	1.3.1
	Title	Summary of Product Characteristics (SPC)
	Element	m1-3-1-spc
	Directory	module-1/eu/common/pi/spc
	Comment	This folder contains all the SPC documents in an accepted narrative file format per language, e.g. spc-en.rtf, spc-nl.rtf, etc.
12	Number	1.3.1.1
	Title	SPC in English
	Element	m1-3-1-spc
	File	module-1/eu/common/pi/spc/spc-en.pdf
	Comment	All SPCs in the different languages are treated in the same way, where the language of the file is specified by the two-character language code from ISO-639. Files can be in an accepted narrative file format.
13	Number	1.3.2
	Title	Labeling
	Element	m1-3-2-label
	Directory	module-1/eu/common/pi/label
	Comment	Labeling is defined as the information on the immediate packaging or the information on the blister or strip
14	Number	1.3.2.1
	Title	Information on the immediate packaging, e.g. bottle
	Element	m1-3-2-1-impack
	Directory	module-1/eu/common/pi/label/impack
	Comment	This folder contains all the immediate pack documents in PDF per language, e.g. impack-en.pdf
15	Number	1.3.2.1.1
	Title	Information on the immediate packaging in English
	Element	m1-3-2-1-impack
	File	module-1/eu/common/pi/label/impack/impack-en.pdf
	Comment	All documents with immediate packaging information in the different languages are treated in the same way, where the language of the file is specified by the two-character language code from ISO-639. Files can be in an accepted narrative file format.

16	Number	1.3.2.2
	Title	Information on blister packs
	Element	m1-3-2-2-blister
	Directory	module-1/eu/common/pi/label/blister
	Comment	This folder contains all the blister pack documents in PDF or RTF per language, e.g. blister-en.pdf
17	Number	1.3.2.2.1
	Title	Information on blister packs in English
	Element	m1-3-2-2-blister
	File	module-1/eu/common/pi/label/blister/blister-en.pdf
	Comment	All documents with outer packaging information in the different languages are treated in the same way, where the language of the file is specified by the two-character country code. Files can be in an accepted narrative file format.
18	Number	1.3.3
	Title	Patient Information Leaflet (PIL)
	Element	m1-3-3-pil
	Directory	module-1/eu/common/pi/pil
	Comment	This folder contains all the PIL documents in an accepted narrative file format per language, e.g. pil-en.rtf, pil-nl.rtf, etc.
19	Number	1.3.3.1
	Title	PIL in English
	Element	m1-3-3-pil
	File	module-1/eu/common/pi/pil/pil-en.rtf
	Comment	All PILs in the different languages are treated in the same way, where the language of the file is specified by the two-character language code from ISO-639. Files can be in an accepted narrative file format.
20	Number	1.3.4
	Title	Mock-ups = Information on outer packaging, e.g. carton box
	Element	m1-3-4-outer
	Directory	module-1/eu/common/pi/outer
	Comment	This folder contains all the outer-pack documents in an accepted narrative format file per language, e.g. outerpack-en.pdf
21	Number	1.3.4.1
	Title	Outer packaging in English
	Element	m1-3-4-outer
	File	module-1/eu/common/pi/outer/outer-en.pdf
	Comment	Outer-packaging is similar to mock-up. If a higher resolution is required, this graphic file can be in JPEG, GIF, PNG or SVG.
22	Number	1.3.5
	Title	SPCs already approved in the Member States
	Element	m1-3-5-spc-approved
	Directory	module-1/eu/common/pi/spc-approved
	Comment	This folder contains all the SPC documents in an accepted narrative file format per language, e.g. spc-en.rtf, spc-nl.rtf, etc. already accepted in the Member States
23	Number	1.3.5.1
	Title	Approved SPC in English
	Element	m1-3-5-spc-approved
	File	module-1/eu/common/pi/spc-approved/spc-en.pdf
	Comment	All approved SPCs in the different languages are treated in the same way, where the language of the file is specified by the two-character language code from ISO-639. Files can be in an accepted narrative file format.

24	Number	1.4
	Title	Information about the Experts.
	Element	m1-4-expert
	Directory	module-1/eu/common/expert
	Comment	
25	Number	1.4.1
	Title	Quality Expert
	Element	m1-4-1-expert-quality
	File	module-1/eu/common/expert/expert-quality.pdf
	Comment	Curriculum vitae, information and signature of the Expert
26	Number	1.4.2
	Title	Non-clinical Expert
	Element	m1-4-1-expert-nonclin
	File	module-1/eu/common/expert/expert-nonclin.pdf
	Comment	Curriculum vitae, information and signature of the Expert
27	Number	1.4.3
	Title	Clinical Expert
	Element	m1-4-1-expert-clin
	File	module-1/eu/common/expert/expert-clin.pdf
	Comment	Curriculum vitae, information and signature of the Expert
28	Number	1.5
	Title	Specific information on the type of application
	Element	m1-5-specific
	Directory	module-1/eu/common/specific
	Comment	
29	Number	1.5.1
	Title	Information for bibliographic applications under Art.4.8 (a)(ii) of Dir 65/65
	Element	m1-5-1-specific-bibliographic
	File	module-1/eu/common/specific/specific-bibliographic.pdf
	Comment	
30	Number	1.5.2
	Title	Information for abridged "generic" applications under Art.4.8 (a)(iii) of Dir 65/65, 1^{e} and 2^{e} paragraph
	Element	m1-5-2-specific-abridged
	File	module-1/eu/common/specific/specific-abridged.pdf
	Comment	
31	Number	1.6
	Title	Annex: Environmental risk assessment
	Element	m1-6-annex
	File	module-1/eu/common/annex.pdf
	Comment	

32	Number	1.7
	Title	Other information
	Element	m1-7-other
	Directory	module-1/eu/common/other
	Comment	Use this level to submit leaf documents that do not fit into one of the m1-regional tags; some examples are given below; in other cases node extension can be used
33	Number	1.7.1
	Title	Cover letter for the submission
	Element	m1-7-1-cover
	File	module-1/eu/common/other/cover.pdf
	Comment	
34	Number	1.7.2
	Title	Letters of authorization
	Element	m1-7-2-author
	File	module-1/eu/common/other/author.pdf
	Comment	
35	Number	1.7.3
	Title	GMP certificate
	Element	m1-7-3-gmp
	File	module-1/eu/common/other/gmp.pdf
	Comment	

Table 4: Leaf Element attribute list

Element	Attribute	Description/Instructions	Example
<leaf>		A leaf corresponds to a file. One or more child leaf elements may be submitted for a parent table of content tag.	
	ID	Unique identifier for this location in the XML instance.	
	application-version	The version of the software application that was used to create this file.	**Acrobat 5**
	version	The file senders internal version number or version identification for the report.	**V23.5**
	font-library	The commercial name of the font or font library needed to properly view the submitted file.	

	operation	Indicates the operation to be performed on the "modified-file". Select one of the following valid values:
		`new`
		`replace`
		`append`
		`delete`
		See the section Operation Attribute in appendix 6 of the eCTD Specification for details on the meaning of these values
			new

	modified-file	The name of the file to be modified as indicated in the "operation" attribute. This file name should include the relative path to the file. If no file is being modified, then do not supply the "modified-file" attribute.	N/A
	checksum	The checksum value for the file being submitted.	**e854d3002c02a61fe5cbe926fd97b001**
	checksum-type	The checksum algorithm	**MD5**
	keywords	Significant word(s) used in indexing or cataloguing	
	xmlns:xlink	http://www.w3c.org/1999/xlink	
	xlink:type	Fixed value of "simple".	**Simple**
	xlink:role	Not Currently Used	
	xlink:href	Provide the pointer to the actual file. Use the relative path to the file and the file name.	**/0000/module-1/eu/common/other/ cover.pdf**
	xlink:show	Not Currently Used.	
	xlink:actuate	Not Currently Used	
	xml:lang	The primary language of the file. Use ISO-639 standard language abbreviations	**en**

Creating the XML EU Index Submission

The agency number should be used as the folder name in the top-level directory. For example, if the agency number is RVG 123456, the top-level directory would be named “rvg-123456”. The new application and subsequent submissions in the form of supplemental information, variations, renewals, etc. should use the same top-level folder name. Each submission should be differentiated by a subfolder named according to the sequence number of the submission to the EU regulatory agency. The agency number and sequence number should be included in the “envelope” element of the EU Index instance. The first subfolder 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 Index 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 <m1-7-1-cover> to submit a file containing the cover letter for the submission.
2. Create a child <leaf> element for the <m1-7-1-cover> tag. If more than one file belongs at this level, you may create more than one <leaf> element under the tag.
3. Provide the relative location and file name of the actual file containing the cover letter using the “xlink:href” attribute for the <leaf> element.
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 Table 4.

Instructions for a Simple New Submission

The following XML fragment demonstrates the submission of a cover letter as a PDF file.

```
<?xml version = "1.0" encoding = "iso-8859-1" ?>
<!DOCTYPE eu:eu-backbone SYSTEM "file://util/dtd/eu-index.dtd">

<eu:eu-backbone
  xmlns:eu          = “http://emea.int.eu”
  xmlns:xlink       = “http://www.w3c.org/1999/xlink“
  dtd-version       = "0.52"
>

 <envelope>
        <applicant>Super Pil Inc.</applicant>
        <agency>Medicines Evaluation Board</agency>
        <agency-number>RVG 123456</agency-number>
        <product-name>Wonder Pil</product-name>

        <submission
                type                    = "new"
                submission-date    = "2001-11-01"
                sequence-number = "0000"
        />
 </envelope>

 <m1-eu-common>
        <m1-7-other>
                <m1-7-1-cover>
                        <leaf
                          operation    = "new"
                          xmlns:xlink  =“http://www.w3c.org/1999/xlink”
                          xlink:type     = "simple" xlink:href = "module-1/eu/common/other/cover.pdf"
                        >
                                <title>Original cover letter</title>
```

```
                    </leaf>
                </m1-7-1-cover>
        </m1-7-other>
  </m1-eu-common>
</eu:eu-backbone>
```

This submission includes the file “cover.pdf” in the relative directory “module-1/eu/common/other” for the current submission sequence number, “0000” in this example. The file is “new” and has a descriptive name of “Original cover letter”.

If this is the first submission for RVG 123456, all the folders and files in this submission are in the rvg-123456\0000 directory or folder and below.

Instructions for an Amendment, Supplement or Variation

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

To replace a file, add the replacement file <leaf> element under the same tag element as the original file. If this is the second submission for RVG 123456, all the files in this submission are in the rvg-123456\0001 folder and below.

```
<?xml version = "1.0" encoding = "iso-8859-1" ?>
<!DOCTYPE eu:eu-backbone SYSTEM "file://util/dtd/eu-index.dtd">

<eu:eu-backbone
  xmlns:eu        = “http://emea.int.eu”
  xmlns:xlink     = “http://www.w3c.org/1999/xlink“
  dtd-version     = "0.52"
>

  <envelope>
        <applicant>Super Pil Inc.</applicant>
        <agency>Medicines Evaluation Board</agency>
        <agency-number>RVG 123456</agency-number>
        <product-name>Wonder Pil</product-name>
        <submission
           type                 = "supplemental"
           submission-date      = "2001-11-20"
           sequence-number      = "0001"
        />

  </envelope>
  <m1-eu-common>
        <m1-3-pi>
                <m1-3-1-spc>
                        <leaf
                          operation       = "replace"
                          xmlns:xlink     = “http://www.w3c.org/1999/xlink”
                          xlink:type      = "simple"
                          xlink:href      = "module-1/eu/common/pi/spc/spc-nl.pdf"
                          modified-file   = "0000/module-1/eu/common/pi/spc/spc-nl.pdf"
                          version         = "v2"
                        >
                                <title>SPC version 2</title>
                        </leaf>
                </m1-3-1-spc>
        </m1-3-pi>
  </m1-eu-common>
</eu:eu-backbone>
```

Business protocol

General

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 structure. The exact description has to be provided if necessary 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 physical media like CD-ROMs:

1. the actual submission of the physical media on which the application is contained should be accompanied by a signed, paper copy of the cover letter (the content of this cover letter is defined in the eCTD Specification Document appendix 5 as is the packaging of the media units)
2. the agency acknowledge the proper receipt and the result of the validation process (technical (e.g. virus check, XML check, etc.) and content based) to the company 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 through a secure email connection for all related subsequent submissions.
It is evident that once communication will be purely electronic (e.g. over a secure connection through the Internet), a defined data interchange standard should be available.

Electronic signatures

A crucial part of pure electronic communications between the pharmaceutical industry and regulatory agencies will be the use of electronic signatures. Currently the EU is developing a strategy to implement electronic signatures.

Change control.

For all suggested changes to the ICH eCTD Specification Document, the ICH change control procedure should be used. The relevant details on a contact address and e-mail address for the EU can be found in the ICH eCTD Specification Document, appendix 5. Changes to this EU guideline on Module 1 should be forwarded to the same e-mail address: esubmission@emea.eu.int
The Telematics Implementation Group on Electronic Submissions (TIGes) will act as the EU body responsible for the change control at the EU level.

ANNEX A: EU Index DTD

```
<!--
PUBLIC "-//EMEA//DTD eCTD EU Backbone 0.52//EN"
SYSTEM "http://esubmission.eudra.org/ectd/eu-index.dtd"
In the eCTD File Organisation: "util/dtd/eu-index.dtd"

Editors:
 C.A. van Belkum, MEB, ca.v.belkum@cbg-meb.nl, +31 70 356 7469
 M.T. Carrasco Benitez, EMEA, manuel.carrasco@emea.eu.int, +44 20 7418 8645

27 March 2002

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

Abbreviations of the identifiers:
admin : adminstration
appli : application
autho : authorisation
certi : certificate
envi  : environment
imme  : immediate-pack
info  : information
pack  : packaging
req   : requirements
spec  : specific
var   : variation
-->
<!-- ============================================================ -->
<!-- entities -->
<!ENTITY % att " ID ID #IMPLIED xml:lang CDATA  #IMPLIED">
<!ENTITY % leaf-node " ((leaf | node-extension)*)">
<!ENTITY % leaf-node-simple "  (leaf | node-extension)* ">
<!-- ============================================================ -->
<!-- root element -->
<!ELEMENT eu:eu-backbone (envelope, m1-eu*)>
<!ATTLIST eu:eu-backbone
   xmlns:eu CDATA #FIXED "http://emea.eu.int"
   xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
   xml:lang CDATA #IMPLIED
   dtd-version CDATA #FIXED "0.52"
>
<!-- ============================================================ -->
<!ENTITY % envelope-module SYSTEM "eu-envelope.mod">
%envelope-module;
<!-- ============================================================ -->
<!ELEMENT m1-eu (m1-eu-common, m1-eu-country*, %leaf-node-simple;)>
<!ATTLIST m1-eu
   %att;
>
<!ELEMENT m1-eu-common (m1-2-application?, m1-3-pi?, m1-4-experts?, m1-5-specific?, m1-6-
annex?, m1-7-other?, %leaf-node-simple;)>
<!ATTLIST m1-eu-common
   %att;
>
<!ELEMENT m1-2-application ((m1-2-1-part1a | m1-2-2-variation | m1-2-3-renewal)?, %leaf-
node;)>
<!ATTLIST m1-2-application
   %att;
>
<!ELEMENT m1-2-1-part1a %leaf-node;>
<!ATTLIST m1-2-1-part1a
   %att;
>
<!ELEMENT m1-2-2-variation %leaf-node;>
<!ATTLIST m1-2-2-variation
   %att;
>
<!ELEMENT m1-2-3-renewal %leaf-node;>
<!ATTLIST m1-2-3-renewal
   %att;
>
```

```
<!ELEMENT m1-3-pi (m1-3-1-spc?, m1-3-2-label?, m1-3-3-pil?, m1-3-4-outer?, m1-3-5-spc-
approved?, %leaf-node;)>
<!ATTLIST m1-3-pi
   %att;
>
<!ELEMENT m1-3-1-spc %leaf-node;>
<!ATTLIST m1-3-1-spc
   %att;
>
<!ELEMENT m1-3-2-label (m1-3-2-1-impack?, m1-3-2-2-blister?, %leaf-node;)>
<!ATTLIST m1-3-2-label
   %att;
>
<!ELEMENT m1-3-2-1-impack %leaf-node;>
<!ATTLIST m1-3-2-1-impack
   %att;
>
<!ELEMENT m1-3-2-2-blister %leaf-node;>
<!ATTLIST m1-3-2-2-blister
   %att;
>
<!ELEMENT m1-3-3-pil %leaf-node;>
<!ATTLIST m1-3-3-pil
    %att;
>
<!ELEMENT m1-3-4-outer %leaf-node;>
<!ATTLIST m1-3-4-outer
   %att;
>
<!ELEMENT m1-3-5-spc-approved %leaf-node;>
<!ATTLIST m1-3-5-spc-approved
    %att;
>
<!ELEMENT m1-4-experts (m1-4-1-expert-quality?, m1-4-2-expert-nonclin?, m1-4-3-expert-clin?,
%leaf-node;)>
<!ATTLIST m1-4-experts
   %att;
>
<!ELEMENT m1-4-1-expert-quality %leaf-node;>
<!ATTLIST m1-4-1-expert-quality
    %att;
>
<!ELEMENT m1-4-2-expert-nonclin %leaf-node;>
<!ATTLIST m1-4-2-expert-nonclin
    %att;
>
<!ELEMENT m1-4-3-expert-clin %leaf-node;>
<!ATTLIST m1-4-3-expert-clin
    %att;
>

<!ELEMENT m1-5-specific ((m1-5-1-specific-bibliographic | m1-5-2-specific-abridged)?, %leaf-
node;)>
<!ATTLIST m1-5-specific
   %att;
>
<!ELEMENT m1-5-1-specific-bibliographic %leaf-node;>
<!ATTLIST m1-5-1-specific-bibliographic
    %att;
>
<!ELEMENT m1-5-2-specific-abridged %leaf-node;>
<!ATTLIST m1-5-2-specific-abridged
    %att;
>
<!ELEMENT m1-6-annex %leaf-node;>
<!ATTLIST m1-6-annex
   %att;
>
<!ELEMENT m1-7-other (m1-7-1-cover?, m1-7-2-author?, m1-7-3-gmp?, %leaf-node-simple;)>
<!ATTLIST m1-7-other
   %att;
>
<!ELEMENT m1-7-1-cover %leaf-node;>
<!ATTLIST m1-7-1-cover
   %att;
>
<!ELEMENT m1-7-2-author %leaf-node;>
```

```
<!ATTLIST m1-7-2-author
   %att;
>
<!ELEMENT m1-7-3-gmp %leaf-node;>
<!ATTLIST m1-7-3-gmp
   %att;
>
<!ELEMENT m1-eu-country %leaf-node;>
<!ATTLIST m1-eu-country
   %att;
   country CDATA #REQUIRED
>
<!-- ============================================================ -->
<!ELEMENT node-extension (title, (leaf | node-extension)+)>
<!ATTLIST node-extension
   ID ID #IMPLIED
   xml:lang CDATA #IMPLIED
>
<!-- ============================================================ -->
<!--
leaf content is based on the ich-ectd-1-0.dtd
see the Step 2 eCTD Specification Document, Brussels, February 2002

If the ich-ectd.dtd is modularized, this could be just included.
Hence, one is certain that the common and EU leaf are the same.
-->
<!ELEMENT leaf (title, link-text?)>
<!ATTLIST leaf
   ID ID #IMPLIED
   application-version CDATA #IMPLIED
   version CDATA #IMPLIED
   font-library CDATA #IMPLIED
   operation (new | append | replace | delete) #REQUIRED
   modified-file CDATA #IMPLIED
   checksum CDATA #IMPLIED
   checksum-type CDATA #IMPLIED
   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 (new | replace | embed | other | none) #IMPLIED
   xlink:actuate (onLoad | onRequest | other | none) #IMPLIED
   xml:lang CDATA #IMPLIED
>
<!ELEMENT title (#PCDATA)>
<!ATTLIST title
   ID ID #IMPLIED
>
<!ELEMENT link-text (#PCDATA | xref)*>
<!ATTLIST link-text
   ID ID #IMPLIED
>
<!ELEMENT xref EMPTY>
<!ATTLIST xref
   ID ID #IMPLIED
   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 (new | replace | embed | other | none) #IMPLIED
   xlink:actuate (onLoad | onRequest | other | none) #IMPLIED
>
<!-- end of file -->
```

```
<!--
SYSTEM "http://esubmission.eudra.org/ectd/eu-envelope.mod"
In the eCTD File Organisation: "util/dtd/eu-envelope.mod"

Editors:
 C.A. van Belkum, MEB, ca.v.belkum@cbg-meb.nl, +31 70 356 7469
 M.T. Carrasco Benitez, EMEA, manuel.carrasco@emea.eu.int, +44 20 7418 8645

28 February 2002

Abbreviation of the submission types:
 presub  : pre-submission
 new     : new application
 sup     : supplemental information after questions
 type1   : variation type I
 type2   : variation type II
 psur    : Periodic Safety Update Report
 renewal : renewal
 dmf     : Drug Master File
-->

<!ELEMENT envelope (
 agency ,
 agency-number ,
 submission ,
 applicant ,
 product-name ,
 approval-date
)>

<!ELEMENT agency        (#PCDATA)>
<!ELEMENT agency-number (#PCDATA)>
<!ELEMENT submission    EMPTY    >
<!ELEMENT applicant     (#PCDATA)>
<!ELEMENT product-name  (#PCDATA)>
<!ELEMENT approval-date (#PCDATA)>

<!ATTLIST submission
   type (
      presub
    | new
    | sup
    | type1
    | type2
    | psur
    | renewal
    | dmf
   ) #REQUIRED
   date            CDATA #REQUIRED
   sequence-number CDATA #REQUIRED
>
<!--  end of file -->
```