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# EU Module 1 eCTD Specification

Version 2.4 – Draft

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## 17  Document Control

### 18  *Change Record*

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|---|---|---|---|

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21 **Reviewers**

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| 0.1-0.3 | EU Regulators | EU Regulatory Authorities, EMEA |
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| 0.9 | EU regulators | EU Regulatory Authorities, EMEA |
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| 0.92 | EU regulators | EU Regulatory Authorities (members TIGes and NtA) |
| 0.95.1 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, Pharma, other interested parties |
| 0.95.2 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, Pharma, other interested parties |
| 0.95.3 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, Pharma, other interested parties |
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| 1.3 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, Pharma, other interested parties |
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| 2.1.5 | eSubmission CMB | EU Regulatory Authorities (NCAs and EMA), EFPIA, EGA, other interested parties |
| 2.1.5 | TEAB | Telematic Enterprise Architecture Board (NCAs and EMA) |
| 2.1.5 | IT Directors | IT Directors of all NCAs |
| 2.4 | EU-Regulators, interested parties | Public consultation |

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# Glossary of Terms

| Term | Definition |
|---|---|
| Applicant | A pharmaceutical company or its agent that is submitting information in support of an *application*. |
| Applicant's Information | Regulatory information submitted by an *applicant* for, or to maintain, a marketing authorisation that falls within the scope of this guidance document. |
| eCTD Application | A collection of electronic documents compiled by a pharmaceutical company or its agent in compliance with European legislation and guidelines in order to seek a marketing authorisation or any amendments thereof.  An *eCTD application* may comprise a number of *regulatory activities*.  In the EU an eCTD application may comprise several dosage forms and strengths, all under one invented product name. This is understood to be equivalent to a Global Marketing Authorisation according to Art. 6 para 2 Dir. 2001/83/EC as amended. Some review tools describe such a collection as a application (a term which will not be used in this document). |
| Procedure | A Community registration procedure for the authorisation of medicinal products in the European Community.  There are 4 types of procedure that operate within the EC – Centralised, Decentralised, Mutual Recognition and National. |
| Regulatory Activity | A collection of *sequences* covering the start to the end of a specific business process, e.g. a MA application or Type II variation |
| Sequence | A single set of information and / or electronic documents submitted at one particular time by the applicant as a part of, or the complete, *Application.* .Any collection of content assembled in accordance with the eCTD specification (ICH and EU) will be described using metadata as defined by the EU envelope. |
| Submission Type | The submission type describes the *regulatory activity* to which the content will be submitted. |
| Submission Unit | The submission unit element of the envelope metadata set describes the content at a lower level (a "sub-activity") which is submitted in relation to a defined regulatory activity such as the initial submission, the applicant response to validation issues or list of questions or any other additional information. |

## Introduction

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

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

## EU Module 1: Regional Information

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

The following items listed in the Notice to Applicants should be included for an initial submission:
  – a cover letter,
  – a comprehensive table of contents[1],
  – an application form,
  – product information documents,
  – information on the experts,
  – specific requirements for different types of applications (if required),
  – an environmental risk assessment,
  – information relating to orphan market exclusivity (if required),
  – information relating to pharmacovigilance,
  – information relating to clinical trials (if required),
  – information relating to paediatrics.

In addition, other items such as answers to regulatory questions, rationale for variations and renewal documentation could also be included in Module 1.

It should be noted, that for subsequent submissions in the lifecycle of a medicinal product, e.g. for a variation, not all of the above mentioned types of document need to be included in Module 1. Consult the various legal documents for guidance on the exact documents to be submitted in such a case.

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.

The acronym 'EMEA' will remain in use in the Product Numbers, however it will be changed to EMA in the various technical texts.

## Regional File Formats

### *Module 1*

The file formats that can be included in Module 1 are given in Table 1. In addition to the common format PDF, as defined by the ICH eCTD Specification Document, XML and image formats are also accepted on an ad hoc basis. Note that all PDF files included in an eCTD (irrespective of the module) should be v1.4, v1.5, v1.6 or v1.7 (see ICH Q&A for further detail re PDF version acceptability), except where there is an agency-specific requirement for a later version (e.g. for an application form). Although the use of the file formats defined in Table 1 are mandatory, regulatory authorities and applicants could agree on the use of other formats for Module 1 content provided outside of the eCTD

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

124 in the working-documents folder. For example, proprietary format MS Word is requested by some
125 agencies for Product Information documents in Section 1.3. These documents, if requested, should
126 not be referenced in the eCTD backbone, and should normally be provided in addition to the PDF
127 versions (Note: Track changed Product Information provided in Word format is not required to be
128 provided in PDF format within the eCTD, An exception to this rule is in the provision of either product
129 labelling or risk management plan documentation in the Centralised Procedure, where the tracked
130 changes version of the document in PDF format should be placed inside the eCTD, alongside the
131 clean, non-tracked version.). Guidance should be referred to regarding the provision of MS Word and
132 other requested documents (e.g. the Harmonised Technical Guidance for eCTD Submissions in the
133 EU).

134 Table 1 Acceptable file formats for Module 1

| Document | File Format | Remark |
|---|---|---|
| Cover letter | XML*, PDF | PDF preferably generated from electronic source. |
| Administrative forms:<br>• Application form and its annexes | XML*, PDF | Documents should be generated from electronic source documents, any signature may be embedded as a graphic file in the PDF text if desired, although this is not always necessary as the hard paper copy, if required by the receiving agency, contains the legally binding signature. |
| • Variation application form incl. background for the variation | XML*, PDF | The use of eAF is mandatory for Centralised Procedure applications (MAA, variation, renewal) from 1 July 2015 and for MRP/DCP/National from 1 January 2016. After these dates the paper forms will no longer be accepted. |
| • Renewal form and its annexes | XML*, PDF | |
| Product Information:<br>• Product information text** | XML*,PDF | If a higher resolution is necessary for the mock-ups, use JPEG, GIF, PNG or SVG on a case-by-case basis. |
| • Packaging mock-ups | PDF | |
| • Reference to specimens | PDF | |
| Other | XML*, PDF | PDF preferably generated from electronic source. |

135
136 * =XML format could replace PDF format whenever a structured EU exchange standard exists for the
137 content in the specific CTD location
138 ** = SmPC, Package Leaflet and labelling
139

## *Modules 2 to 5*

141 No additional file formats are defined for Modules 2 to 5 other than those mentioned in the ICH eCTD
142 Specification Document.
143

# Use of Electronic Signatures

145 Currently, the use of digital signatures for electronic submissions within the EU is not fully supported.
146 Some agencies continue to request wet signed documents and others will accept the log-in
147 credentials for portals as a sufficient authentification. Please refer to the Harmonised Technical
148 Guidance for eCTD Submissions in the EU for information on the use of electronic signatures.
149

150

## Handling of Empty or Missing eCTD Sections

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

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

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

## Updating backbone attributes/metadata

It is not possible to update XML backbone attributes such as 'manufacturer' during the eCTD lifecycle, nor is it necessary to attempt workarounds such as deleting existing documents and resubmitting them with new attributes. The recommendation is to retain the obsolete entry and to rely on the document content to explain the current details. The sole exception to this rule is the EU envelope "submission type" attribute, which can be updated to support a mid-lifecycle change in submission type from one variation type to another (under the variation regulation).

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

## General Architecture of Module 1

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

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

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

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

203 *Envelope*

204 The "`eu-envelope`" element is designed to be used for all types of submissions (MAAs, variations,
205 renewals, etc.) for a given medicinal product and will mainly be used for the first simple processing at
206 the agency level. The envelope provides meta-data at the eCTD application and sequence level. A
207 description of each "envelope" element is provided in Appendix 1 of this specification.

209 For Centralised Procedure submissions, the "`eu-envelope`" element should contain a single
210 "`envelope` "element with the country attribute value set to 'EU-EMA'. For all other procedures, the
211 "`eu-envelope`" element should contain a separate "`envelope`" element for each Member State
212 involved in the procedure that is going to receive that particular sequence, and each envelope country
213 attribute should be set to the country value of the receiving Member State. Note that the value
214 'common' cannot be used in the envelope.

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

221 • For worksharing submissions including PSUSA and referrals
222 Here, the submission 'mode' value will be 'worksharing' and the high-level number is a
223 worksharing number, the PSUSA number or referral number;

225 • For submissions of grouped Type 1A variations that affect multiple marketing authorisations
226 Here, the submission 'mode' will be 'grouping' and the high-level number is group
227 number/report' number. Please refer to the annex and associated guidance for further details
228 of this high-level number. Examples of 'single', 'grouping' and 'worksharing' submissions are
229 provided in the annex to this specification.

231 Such a high-level number, if appropriate, should be provided in addition to the usual product-specific
232 procedure tracking numbers. If the high-level number is required but is not known (e.g. for the first
233 submission of the procedure), this element should be populated with the value 'to be advised'. The
234 relevant number will usually be provided by or obtained from the appropriate tracking system or
235 regulatory agency. In the case of Centralised Procedure this number is always available on the
236 Eligibility Confirmation Letter as 'Product Reference'. E.g. if the Eligibility Confirmation Letter indicates
237 Product number H0002227 please eliminate first digit (0) from H0002227 to reflect H002227 in the
238 envelope. The use of Product Number H/C/xxxxxx is applicable after the Initial MAA has been
239 submitted to the EMA.

241 In the case of Centralised Procedure, it is strongly recommended that when applying for a variation
242 and the procedure number has not yet been allocated, then the term 'to be advised' should be used.
243 If the content of a sequence pertains to more than one submission type (e.g. parallel variations) the
244 highest variation type should be selected as submission type. In this case there will be more than one
245 related sequence. The value of submission unit will be dictated by the content, e.g. "response".

247 For submissions to EDQM, the agency name EU-EDQM and the submission type 'CEP application'
248 need to be selected. The submission unit should be used as appropriate.

251 *m-1-eu*

252 The "`m1-eu`" element of the EU regional DTD is based on the same conceptual approach as the
253 common part of the ICH eCTD DTD. It provides an XML catalogue with meta-data at the leaf level
254 including pointers to the location of files in a directory structure. As for the ICH eCTD DTD,
255 the "`m1-eu`" element maps to the directory structure. (There may at times be what is seen to be an
256 apparently 'redundant' directory structure, but this is necessary in order to be able to use the same file
257 / directory structure for all procedures.) Furthermore, as the same structure will be used during the
258 lifecycle of the submission, the use of country directories even to place a single file in one submission
259 is justified because it could be used to house several files in a subsequent submission, and in doing

260 so the structure would not change. A tabular overview of the directory structure explaining where to
261 place country and language-specific files is provided in Appendix 2 of this specification.
262

## *Directory / File Structure*

264 The EU Module 1 Specification provides a directory and file structure that is strongly recommended:
265 - The same high-level directory structure is used for all 4 procedures (MR, National,
266   Decentralised and Centralised Procedures). This is possible, despite the fact that files for the
267   MR, Decentralised and National Procedures are usually country-specific, whereas files for the
268   Centralised Procedure are usually language-specific.
269 - Country directories are named according to Appendix 2.1.
270 - Language directories are named according to Appendix 2.2.
271 - The recommended directory structure for the use of country and language identifiers is
272   described in Appendix 2. In general, Modules 1.0, 1.2, 1.3.2, 1.3.3, 1.3.4, 1.3.5, 'Additional
273   Data' and 'Responses' have country subdirectories. Module 1.3.1 (Product Information) has
274   both country and language subdirectories.
275   - o For the Centralised Procedure, the country subdirectory is always named either
276     "ema" or "common", irrespective of whether it contains "common" or country folders;
277     language subdirectories in Module 1.3.1 have the appropriate language identifier.
278   - o For MR, Decentralised and National Procedures:
279     - Documents for each country are placed in an appropriately named
280       subdirectory. The folder name "common" should only be used for documents
281       potentially applicable to all EU countries, irrespective of whether they are
282       currently involved in the procedure or not.
283     - In Module 1.3.1, every document should be placed in an appropriately named
284       language subdirectory, even if the country only has one official language.
285       Where a country has more than one official language (e.g. Belgium) separate
286       language subdirectories should be used for each set of documents in a
287       different language.
288     - Should a country have documents in more than one language in a Module
289       other than 1.3.1, then it is recommended to use the VAR (variable) part of the
290       filename to identify the language of the document.
291

## *Node Extensions*

293 Node extensions are a way of providing extra organisational information to the eCTD. The node
294 extension should be visualised as an extra heading in the CTD structure and should be displayed as
295 such when the XML backbone is viewed.
296
297 However, the use of node extensions should be limited to those areas where it is critical.
298 Consideration should be given regarding the impact of the view for the reviewer since the inconsistent
299 use of node extensions can lead to unanticipated effects in the cumulative view of a submission.
300
301 The following rules govern the use of node extensions in the EU:
302 - Node extensions must not be used where ICH-specified sub-headings already exist (e.g.
303   indication, manufacturer, drug substance, drug product are all-ICH specified node
304   extensions).
305 - Node extensions must only be used at the lowest level of the eCTD structure (e.g. a node
306   extension can be used at the level 5.3.5.1 but must not be used at the level 5.3).
307 - Node extensions are mainly to be used to group together documents made up of multiple leaf
308   elements (e.g. a clinical study made up of separate files for the synopsis, main body and
309   individual appendices could be grouped together under a node extension with the Study
310   Identifier as its Title attribute).
311 - Node extensions must be maintained over the entire life of the eCTD lifecycle (e.g. if a node
312   extension is used in Sequence 0000 to group files for a study report in Module 5.3.5.1, then
313   any files submitted in a later sequence must also be placed under a node extension, even if
314   only one file is submitted).

11

315   •   Node extensions may be nested as this is allowed by the eCTD DTD. However, as noted in
316       Bullet 2, the first node extension must be at the lowest level in the eCTD structure (e.g. in
317       Module 5.3.7 a node extension may be added to group together files with the Study Identifier
318       as Title attribute). Further node extensions may be added as children of the Study Identifier
319       node, separating CRFs from individual patient listings.
320   •   The content associated with a node extension can be placed in a separate sub folder in the
321       submission; this is recommended for studies in Module 5 where study reports are provided as
322       multiple files. However, there is no specific requirement for an additional subfolder. For
323       example, if node extensions are used to further define 'm1-responses', additional folders
324       under 'm1/eu/responses/cc' are not recommended. Instead, for navigational support the
325       variable part of the file name can be used as outlined in the next section.

## *File Naming Convention*

327 File names in Module 1 follow one of two conventions.
328
329 Country-specific items in sections *1.0; 1.2; 1.3; m1-responses* and *m1-additional-data* have the
330 general structure CC-FIXED-VAR.EXT, where CC is a country code used in some CTD modules,
331 FIXED is a defined component of the filename based on the CTD section and VAR is an additional
332 optional variable component. EXT represents the file extension. Components are separated by a
333 hyphen (except the dot for the file extension). No spaces should be used within each component but
334 hyphens can be used in the variable part to separate several words.
335
336 Fixed components are highly recommended. The variable component is optional and should be used
337 as appropriate to further define these files. The variable component, if used, should be a meaningful
338 concatenation of words with the option of hyphens for separators and should be kept as brief and
339 descriptive as possible. File extensions in line with this specification should be applied as applicable.
340
341 The first component in a file name should be the country code, as per Appendix 2.1, except when the
342 document is valid for all countries in all procedures, as per Appendix 2. The second component
343 should be the document type code, as per Appendix 2 and 2.3. The third component if necessary
344 should be the variable component. In cases where differentiation is needed (e.g. between 1.5mg and
345 15mg) the word 'point' written in full (i.e. '1point5mg') or a hyphen can be used (i.e.'1-5mg').
346
347 There are no recommendations for variable components in this specification. The format of the file is
348 indicated by the file extension. File names should always be in lowercase, in line with the ICH eCTD
349 specification.
350
351 Examples:
352       fr-cover.pdf
353       be-form.xml
354       it-form-annex1.pdf
355       pt-form-proofpayment.pdf
356       uk-outer-tablet10mg.pdf
357       ema-combined-tablet1-5mg.pdf
358       ema-combined-tablet10mgannotated.pdf
359       nongmo.pdf
360
361 In m1-responses/cc, the recommendation is to use cc-responses-<regulatory activity type identifier>-
362 <timeline identifier>-<content identifier>.pdf, using the -var component of the filename to define the
363 content. It is recommended to use the variable component of the filename and the leaf title, to present
364 the information clearly to the assessor.
365
366 Examples:
367
368       common-responses-maa-d106-clin.pdf    Leaf title: Day 106 Clinical Responses, MAA
369       common-responses-var05-d59-qual.pdf   Leaf title: Day 59 Quality Responses, Var 05
370
371

372 Non-country specific items in Sections *1.4; 1.5; 1.6; 1.7; 1.8; 1.9 and 1.10* have fixed file names, as
373 defined in [Appendix 2](#).

## *Folder and File Name Path Length*

375 The overall folder and file name path length starting from the sequence number should not exceed
376 180 characters, for any file in any module. This is an EU regional requirement, and it is acknowledged
377 that this is less than the ICH agreed overall path length.
378

# Business Protocol

380 It is clear that the detailed business process between industry and a regulatory agency in the EU
381 cannot be completely harmonised due to the differences in organisation and processes. The exact
382 description has to be provided by the EMA, EDQM or the individual Member States. However, a few
383 common steps can be identified and will be detailed in the Harmonised Technical Guidance for eCTD
384 Submissions in the EU. The EMA, EDQM and most national agencies are unable to provide positive
385 feedback of technically valid submissions. However, if there is any problem experienced during the
386 upload of the sequence, agencies will promptly inform the applicants. Please note that the EMA
387 provides automated feedback (acknowledgement) of technical validation for submissions received via
388 their [eSubmission Gateway](#) and Web Client.
389

# Universal Unique Identifier

391 In the EU, although the eCTD envelope contains several pieces of information about the eCTD
392 application that the sequence belongs to, such as the procedure number and the trade name, there
393 have been instances when an eCTD sequence has been loaded into the wrong application by the
394 receiving agency. For this reason, all eCTD sequences built in accordance with this revised
395 specification must contain a universal unique identifier (UUID), linking the sequence to the eCTD
396 application to which it belongs.
397
398 The UUID will be built based on ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005. It
399 is a hexadecimal number in the form of xxxxxxxx-xxxx-Axxx-yxxx-xxxxxxxxxxxx, showing 32 digits
400 and 4 hyphens. The 'x' will be replaced by a number or a letter, 'A' will be replaced by a capital
401 character and 'y' will be replaced by a lower case. It is recommended to use randomly generated
402 sections (version 4 of UUID types). Such UUID is represented or example as: 25635f23-a3a4-C4e0-
403 b994-99c5f074960f.
404
405 This structure guarantees uniqueness across applicants and application without further control,
406 accepting a risk of duplication close to zero. The UUID will be generated when creating the first
407 sequence built using this version of the specification, and will be provided in the eCTD envelope. All
408 subsequent sequences for that same application will contain the same UUID. In this way, sequences
409 can be allocated automatically to the correct eCTD application by the receiving agency. The UUID will
410 be transferred to a new MAH and will remain the same also in cases the procedure number changes
411 due to an RMS change. Any independent application with its own life cycle should have its own UUID,
412 e.g. CEP applications or referrals or PIP applications. Instead, redacted clinical study reports or post
413 authorisation measures will relate to an existing application of which the UUID need to be used.
414

# Change Control

416 The EU Module 1 specification is likely to change with time. Factors that could affect the content of
417 the specification include, but are not limited to:
418 • Change in the content of the Module 1 for the CTD, either through the amendment of
419   information, at the same level of detail, or by provision of more detailed definition of content
420   and structure
421 • Change to the regional requirements for applications that are outside the scope of the CTD
422 • Update of standards that are already in use within the eCTD

423     •   Identification of new standards that provide additional value for the creation and/or usage of
424         the eCTD
425     •   Identification of new functional requirements
426     •   Experience of use of the eCTD by all parties, in particular Module 1.
427
428 Details of the change control process and a current Electronic Submission Change Request/Q&A
429 Form are available on the EU eSubmission website.
430

# Appendix 1: The EU Module 1 XML Submission

431

432

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

436 **Appendix 1.1: Envelope Element Description**

437

438 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
439 a specific country.

440

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---------|-----------|-------------------------|---------|------------|------------|
| eu-envelope | | Root element that provides meta-data for the submission. This element may contain several envelopes, which are country specific. | N/A | **Mandatory** | **Unique** |
| envelope | | Parent element for the submission meta-data. This element must be country-specific or in the case of the Centralised Procedure, 'ema' and in the case of CEP applications 'edqm'. | N/A | **Mandatory** | **Repeatable** |
| | country | The country to which the envelope applies (or 'ema' rsp. edqm). | **be** | **Mandatory** | **Unique** |
| identifier | | A UUID as specified by ISO/IEC 11578:1996 and ITU-T Rec X.667 | ISO/IEC 9834-8:2005. The same UUID will be used for all sequences of an eCTD application | 25635f23-a3a4-C4e0-b994-99c5f074960f 596 | **Mandatory** | **Unique** |
| submission | | Provides administrative information associated with the submission. | N/A | **Mandatory** | **Unique** |

15

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---|---|---|---|---|---|
| | type | The type of regulatory activity to which the content will be submitted.. The following are the valid values:<br>▪ `maa` = Marketing Authorisation Application<br>▪ `var-type1a` = Variation Type IA<br>▪ `var-type1ain` = Variation Type IA$_{IN}$<br>▪ `var-type1b` = Variation Type IB<br>▪ `var-type2` = Variation Type II<br>▪ `var-nat` = National variation (e.g. national variation to apply for a pack size that is already registered within an existing MRP/DCP authorisation)<br>▪ `extension` = Extension<br>▪ `psur` = Periodic Safety Update Report (PSUR) which should only be used for PSURs outside of the PSUSA<br>▪ `psusa` = PSUR single assessment procedure<br>▪ `rmp` = Risk Management Plan (outside any procedure)<br>▪ `renewal` = Renewal (yearly or 5-yearly)<br>▪ `pam-sob` = specific obligation related to a post-authorisation measure<br>▪ `pam-anx` = annex II condition related to a post-authorisation measure<br>▪ `pam-mea` = additional pharmacovigilance activity in the risk-management plan related to a post-authorisation measures (RMP) (e.g. interim results of imposed/non-imposed interventional/non-interventional clinical or nonclinical studies)<br>▪ `pam-leg` = legally binding measure related to a post-authorisation measures<br>▪ `pam-sda` = cumulative review following a request originating from a PSUR or a signal evaluation related to a post-authorisation measure<br>▪ `pam-cada` = Corrective Action/Preventive Action related to a post-authorisation measure<br>▪ `pam-p45` = paediatric submissions related to a post-authorisation measure<br>▪ `pam-p46` = paediatric submissions related to a post-authorisation measure<br>▪ `pam-paes` = Submission of a post authorisation efficacy study<br>▪ `pam-rec` = recommendation related to a post-authorisation measures e.g. quality improvement related to a post-authorisation measure<br>▪ `pass107n` = Submission of a post authorisation safety study protocol (according article 107n)<br>▪ `pass107q` = Submission of a post authorisation safety study report (according article 107q) | var-type2 | **Mandatory** | **Unique** |

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---|---|---|---|---|---|
| | | ▪ `asmf` = Active Substance Master File<br>▪ `pmf` = Plasma Master File<br>▪ `referral-20` = Referral under Article 20<br>▪ `referral-294` = Referral under Article 29(4)<br>▪ `referral-29p` = Referral under Article 29 paediatric<br>▪ `referral-30` = Referral under Article 30<br>▪ `referral-31` = Referral under Article 31<br>▪ `referral-35` = Referral under Article 35<br>▪ `referral-53` = Referral under Article 53<br>▪ `referral-107i` = Referral under Article 107i<br>▪ `referral-16c1c` = Referral under Article 16c (1c)i<br>▪ `referral-16c4` = Referral under Article 16c(4)<br>▪ `annual-reassessment` = Annual Reassessment<br>▪ `usr` = Urgent Safety Restriction<br>▪ `clin-data-pub-rp` = Clinical data for publication – Redacted Proposal<br>▪ `clin-data-pub-fv` = Clinical data for publication – Final Version<br>▪ `paed-7-8-30` = Paediatric submission related to a paediatric investigational plan according to article 7, 8 or 30 of the Regulation<br>▪ `paed-29` = Paediatric submission post approval once a paediatric investigational plan has been performed<br>▪ `paed-45`= Paediatric submission according to article 45 of the Regulation<br>▪ `paed-46`= Paediatric submission according to article 46 of the Regulation<br>▪ `article-58` = Article 58 (to be used for an initial application)<br>▪ `notification-61-3` = Notification 61(3)<br>▪ `transfer-ma` = Transfer of a marketing authorisation<br>▪ `lifting-suspension` = Lifting of a suspension<br>▪ `withdrawal` = Withdrawal of a marketing authorisation in regard to a strength or form or entirely. This submission type shall not be used to withdraw a regulatory activity.<br>▪ `cep` = Submission that applies to an application on a Certificate of suitability CEP application (EDQM only).<br>▪ `none` = In the exceptional case of reformatting the application no regulatory activity is allowed. Therefore, 'none' must be stated. The submission application unit will identify the sub-activity related to the product. In the submission description some information can be provided to e.g. highlight specific modules being reformatted .<br>N.B. Officially, Roman numerals are used for variations, e.g. Type IA, Type II – the elements must remain Arabic, however. | | | |

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---|---|---|---|---|---|
| | mode | The high-level handling of the information submitted as part of variation(s) and extension applications. The mode should only be used in variation or line extension regulatory activities and must be included in every sequence of that activity. The following are the valid values:<br>▪ `single` = a single regulatory activity (e.g. a Type II variation)<br>▪ `grouping` = a grouped activity (e.g. several variations grouped into a single submission, or a report of type IA variations applicable to one or more marketing authorisations)<br>▪ `worksharing` = an activity subject to a worksharing agreement (e.g. a Type II variation, referral procedures or a PSUSA applicable to more than one marketing authorisation)<br>This information should be identical with the information provided/ticked in the application form. | Single | **Optional**<br><br>*(note that this element must be populated for sequences in variation and line extension activities)* | **Unique** |
| number | | This is the high-level submission number, either a 'worksharing' number, or the high-level submission number to be used when grouping Type IA variations for multiple marketing authorisations. It can also be the PSUSA number or the Referral number.<br>(Note that for submissions affecting multiple MAs, the 'xxxx' used in the submission number is a permanent placeholder, as a single product number cannot be provided).<br>If the Applicant did not obtain the sequential number from the relevant Authorities in advance of their application this field should be populated as "xxxx" as well.<br>For centrally authorised products and Referrals this number must always be obtained in advance by sending an email to PA-BUS@ema.europa.eu.<br>The PSUSA number can be found from the EURD list | For worksharing:<br>**EMEA/H/xxxx/WS/001**<br><br>For grouped IAs:<br>**EMEA/H/C/xxxx/IG/xxxx**<br><br>For PSUSA<br>**PSUSA/00xxxxx/201xxx**<br><br>For Referral:<br>EMEA/H/A-xx/xxxx | **Optional** | **Unique** |
| procedure tracking | | Provides administrative information associated with the application. | N/A | **Mandatory** | **Unique** |

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---|---|---|---|---|---|
| | number | This is any number, used by an agency or the applicant to track the submission, in any procedure, in relation to a particular product. This could be one or more of the following:<br><br>• an MRP/DCP number (e.g. `DE/H/0126/001/MR`),<br><br>• a national procedure number (e.g. `2131577`),<br><br>• the EMA application number (e.g. `EMEA/H/C/000123` or `EMEA/H/C/000123/II/tba` (to be advised), or in case of sequences after 'initial', (e.g. `'response'` or `'supplemental-info'`), `EMEA/H/C/000123/II/14`),<br><br>• an authorisation or licence number, (e.g. `EU/1/00/44/0003 – 0004`),<br><br>• any other number used by an agency to track a submission, (e.g. `PL01234/0003-0004`)<br><br>• a number used by the applicant to manage the submission within their company (e.g. `Pharmacompany123`)<br><br>There must be at least one tracking number identified from the regulators and, in addition, the applicant can choose to include an internal tracking number.<br><br>In the case of Centralised Procedure, it is strongly recommended that when applying for a variation and the procedure number has not yet been allocated , then the term 'to be advised' should be used (no internal number from the applicant should be used).<br><br>It is suggested that if the procedure number has not yet been allocated by the agency then the term 'to be advised' should be used. Applicants should consult national guidance for further information.<br><br>In case of worksharing, or grouped type IA variations applying to more than one MA, a separate eCTD submission must be built for each MA covered by the variation. In the envelope of each of the eCTD submissions, the high-level submission number will be the same, but the individual tracking numbers listed here should be specific to the MA in question, e.g.:<br>For worksharing:<br>• `EMEA/H/C/000123/WS005/`<br>In case of PSUSA<br>• `PSUSA/0000000X/123456`<br><br>In case of Referral procedure<br>• `EMEA/H/A-xx/1234`<br><br>For grouped type 1A variations across multiple MAs:<br>• `EMEA/H/C/000123/IG003/`<br>Please ensure that these WS/IG numbers are always mentioned in the case of supplemental information or corrigendum otherwise the Agency might not be able to process your submission correctly. | See column left | **Mandatory** | **Repeatable** |

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---|---|---|---|---|---|
| submission unit | | Submission unit describes the content at a lower level (a "sub-activity") which is submitted in relation to a defined regulatory activity The following are the valid values:<br>▪ `initial` = Initial submission to start any regulatory activity<br>▪ `validation-response` = For rectifying business validation issues.<br>▪ `response` = submission unit that contains the response to any kind of question, validation issues out-standing information requested by the agency<br>▪ `additional-info` = Other additional Information (could include, for example, missing files) and should only be used, if `validation-response` or `response` is not suitable<br>▪ `closing` = submission unit that provides the final documents in the centralised procedure following the decision of the European Commission<br>▪ `consolidating` = submission unit that consolidates the application after several information in the MRP or DCP handled outside the eCTD but that need to be integrated thereafter to maintain the life cycle properly.<br>▪ `corrigendum` = Correction to the published annexes in the centralised procedure (usually shortly after approval)<br>▪ `reformat` = Intended to support the reformatting of an existing submission application from any format to eCTD, i.e. a baseline eCTD submission containing no content change and which will not be subject to review (see example below). This type will always be used together with the submission type 'none' | response | **Mandatory** | **Unique** |
| applicant | | The name of the company submitting the eCTD. | **PharmaCompany Ltd.** | **Mandatory** | **Unique** |
| agency | | Parent element for the identification of the receiving agency. | N/A | **Mandatory** | **Unique** |
| | code | The identification of the receiving agency (see Appendix 2.4). | **EU-EMA** | **Mandatory** | **Unique** |
| procedure | | Defines the procedure in use with the submission | N/A | **Mandatory** | **Unique** |
| | type | The type of procedure for the submission. The following are the valid values:<br>▪ `centralised` = Centralised Procedure<br>▪ `national` = National Procedure<br>▪ `mutual-recognition` = Mutual Recognition Procedure<br>▪ `decentralised` = Decentralised Procedure | **Centralised** | **Mandatory** | **Unique** |
| invented-name | | The name of the medicinal product. | **WonderPill** | **Mandatory** | **Repeatable** |

**Comment [KM2]:** This term is changed to 'additional-info' to avoid confusing people or maintaining use as previously although the intent has changed..

20

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---|---|---|---|---|---|
| inn | | International Non-proprietary Name, used to identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A non-proprietary name is also known as a generic name. | **Pioglitazone hydrochloride** | **Optional** | **Repeatable** |
| sequence | | This is the sequence number of the submission – this should start at 0000 for the initial submission, and then increase incrementally with each subsequent submission related to the same product e.g. `0000, 0001, 0002, 0003` etc. | **0000** | **Mandatory** | **Unique** |
| related-sequence | | This is the sequence number of previous submission(s) to which this submission relates e.g. the responses to questions to a particular variation. It should never be used together with the submission unit '`initial`' or '`reformat`' | **0001**<br>see guidance below on use and the annex | **Optional** | **Repeatable** |
| submission-description | | This element is used to provide a free text description of the submission. The list below provides additional examples for such a field:<br>▪ For an MAA: Original MAA Application for <Product X> / Response to D120 LOQ<br>▪ For a Type II variation: Please quote the scope of variation from the Application Form<br>▪ For a Type IB variation: Please quote the scope of variation from the Application Form<br>▪ For an Annual Reassessment submission: 4th AR submission for <Product X><br>▪ In case of a referral related submission: Referral under Article YY<br>▪ Response to validation questions<br>▪ Providing supplementary information<br>▪ Dxxx translations | **Response to D120 LOQ** | **Mandatory** | **Unique** |

441
442

443 <u>Example of the use of the Related Sequence and the Submission Unit elements</u>

444

445 The related sequence element is used to identify sequences belonging to the same 'regulatory activity'. A 'regulatory activity' is a logical unit of submission
446 activity (e.g., a Type II Variation) with a defined start and end point (e.g. initial submission to final approval). In the eCTD world, this will consist of all the
447 sequences that together make up the lifecycle of that particular 'regulatory activity'. The Submission Unit element describes the stage within the regulatory
448 activity, such as initial, response, consolidating.

449

450 The related sequence attribute should always be left blank for new applications or new regulatory activities where the submission unit type is 'initial'. When
451 submitting lifecycle sequences within an existing activity, the related sequence attribute should be populated with the sequence number the regulatory activity
452 has been started with. The submission unit should be populated with the respective term describing the content of the sequence to be filed at that point in
453 time. See below for some illustrative examples.

454

455 It is generally expected that there is usually just one related sequence, but there are occasions where more than one related sequence should be provided:
456 e.g. there are two PAMs (sequence 0050 and sequence 0060) and a single response (sequence 0070) is produced that relates to both PAMs. If more than
457 one different category of activities (submission Types) are referred to (as related sequence), then the "highest category" should be used in the envelope
458 attributes. If any of the related variations were grouped, then 'grouping' should be used. For any of the submission types (regulatory activities) an initial and
459 any of the additional submission unit types can be used, e.g 'response' in case of responses to list of questions or out-standing list of issues. The post
460 authorisation measure may have an initial and additional-info submission unit. The submission description may describe details if this content is related to e.g.
461 an earlier defined obligation or to which day in the procedure the response is assigned to.

462

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

465

| Sequence | Submission description | Submission type | Related sequence | Submission unit | Comment |
|---|---|---|---|---|---|
| 0000 | Original MAA application | maa | <none> | initial | This is the beginning of a new regulatory activity and so the submission unit is 'initial'. The related sequence should never be used together with the submission unit type 'initial' |
| 0001 | Day 121 Responses to questions on the original application | maa | 0000 | response | This is a continuation of the regulatory activity 'maa' initiated in 0000 and so the related sequence points to the beginning of that activity, The submission unit describes the actual contribution 'response' being submitted within maa regulatory activity |
| 0002 | Day 181 Responses to further questions on the original application | maa | 0000 | response | This is a continuation of the regulatory activity 'maa' initiated in 0000 and so the elated sequence points to the beginning of that activity The submission unit describes the actual contribution 'response' being submitted within maa regulatory activity |
| 0003 | Letter of Undertaking (submission type: | maa | 0000 | supplemental-info | This is a continuation of the regulatory activity initiated in 0000 and so the related sequence points to the beginning of that activity. The |

| | | | | | |
|---|---|---|---|---|---|
| | supplemental information) | | | | submission unit describes the actual contribution 'supplemental-info' being submitted within maa regulatory activity |
| 0004 | Type II variation for 'Treatment of Pain' indication | var-type2 | <none> | initial | This is the beginning of a new regulatory activity 'var-type2'and so the submission unit is ,initial'.The related sequence should be left blank. |
| 0005 | Type II variation for a change in manufacturing site (Westferry) | var-type2 | <none> | initial | This is the beginning of another new regulatory activity 'var-type2' and so the submission unit is ,initial'.Again, the related sequence should be left blank. |
| 0006 | Responses to questions on Type II variation for 'Treatment of Pain' indication | var-type2 | 0004 | response | This is a continuation of the regulatory activity initiated in 0004 and so the related sequence points to the beginning of that activity . The submission unit 'response' indicates that this is a response to questions. |
| 0007 | Responses to questions on Type II variation for change in manufacturing site (Westferry) | var-type2 | 0005 | response | As above, but this is a continuation of the regulatory activity initiated in 0005 |
| 0008 | Extension to introduce a new dosage form (iv solution) that amends information provided in the original application and the manufacturing change variation | extension | <none> | initial | This is the beginning of a new regulatory activity and so the submission unit is 'initial', No related sequence is included. |
| 0009 | Updated, agreed, product information taking into account new indication ('Treatment of Pain') | var-type2 | 0004 | response | This is the completion of the new indication ('Treatment of Pain') activity, the related sequence points to the sequence which was 'initial' for this activity, and submission unit indicates that this is a response to questions. |
| 00010 | Updated, agreed product information for the iv formulation | extension | 0008 | consolidating | This is the completion of the new dosage form (iv solution) extension, and so the related sequence is the sequence that started the activity. Submission unit 'consolidating' indicates that further lifecycle 'fixes' have been applied in the sequence. |

For a new regulatory activity, the appropriate submission type should be used. Applicants should refer to the submission type descriptions in the EU Module 1 specification. For the submission unit that initiates a regulatory activity the term 'initial should always be used. For subsequent sequences within that regulatory activity the respective terms should be selected from the submission unit values in the EU M1 specification. The related sequence will be maintained as another way to describe relationships and will be especially meaningful in case of parallel variations.

After the Regulatory Activity has concluded a consolidation of the application may be necessary as in the late phase of the procedure direct exchange of draft documents and interim communication has happened. Final decision, final assessment reports and final versions of the product information texts should be

23

474 submitted within a consolidating sequence.. The submission type 'corrigendum' should only be used in exceptional circumstances to correct information,
475 typically for the product information annexes to be provided in the centralised procedure.
476
477 Tables 1, 2 and 3 provide examples of this convention.
478
479 Table 1: Example of a MAA in the Centralised Procedure

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

480
481

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

| Sequence number | Submission Description | Submission Type | Related Sequence | Submission Unit |
|---|---|---|---|---|
| 0000 | MAA | maa | none | initial |
| 0001 | Validation update | maa | 0000 | response |
| 0002 | Day 106 responses | maa | 0000 | response |
| 0003 | Day 180 responses | maa | 0000 | response |
| 0004 | Day 210 Agreed English product information | maa | 0000 | response |
| 0005 | consolidation after closure of procedure | maa | 0000 | consolidating |

483
484  Table 3: Example of a Variation

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

485
486  Table 4 provides details of which submission unit types should never have a related sequence and which should always have a related sequence

487
488  Table 4: List of Submission Unit and the Use of Related Sequence

| Submission Unit | Should Never Have A Related Sequence | Should Always Have A Related Sequence |
|---|---|---|
| initial | Yes | |
| validation-response | | Yes |
| response | | Yes |
| additional-info | | Yes |
| withdrawal | | Yes |
| closing | | Yes |
| consolidating | | Yes |
| corrigendum | | Yes |
| reformat | Yes | |

489
490
491

25

492  Example of the use of the submission type 'referral-31'

493

494  Referrals according to article 31 are covering in many cases applications from different procedures. So the completing of metadata seems to be difficult and
495  causes inconsistencies. The eCTD envelope will reflect the products involved.  For a pharmacovigilance issue impacting multiple products the referral is run
496  as a centralised procedure. The envelope should indicate the referral procedure number as well as the MR/DC procedure number the submitted sequence
497  relates to.

498

| Envelope for EMA | |
| --- | --- |
| UUID | 25635f23-a3a4-Wce0-r994-99c5f074960f |
| Submission: | Type: Referral-31 |
| Submission: | Mode: worksharing |
| Number | EMEA/H/A-31/9999<br>[This is the referral procedure number] |
| Procedure Tracking Number(s): | PT/H/9999/001-002<br> [This is the original MRP number which will serve to allocate the application correctly] |
| Submission unit | initial |
| Applicant: | Miracle Pharmaceuticals, Inc. |
| Agency: | EMA - European Medicines Agency (EU-EMA) |
| Procedure: | Centralised Procedure<br>[As the referral procedure is centralised.] |
| Invented Name: | Ibuprofen referral |
| INN: | Ibuprofen |
| Sequence: | 0000<br>[The sequence number will be the first one due to the separate referral life cycle]. |
| Related Sequence: | |
| Submission Description: | Referral under Article 31 |

499

500  In case of only one product concerned (but authorised on the European level) the submission mode will turn to single and the submission number will not be
501  filled. The procedure type will also remain MRP and the sequence number must reflect the next free number:

502

| Envelope for CZ | |
| --- | --- |
| UUID | g578w301-a3a4-Vce0-a004-99g5f07T960f |
| Submission: | Type: Referral-31 |
| Submission: | Mode: single |
| Number | |
| Procedure Tracking Number(s): | PT/H/9999/001-002<br>[This is the original MRP number which will serve to allocate the application correctly. In this case no high level procedure number is needed in addition.] |
| Submission unit | initial |
| Applicant: | Miracle Pharmaceuticals, Inc. |

| Agency: | CZ – State Institute for Drug Control (CZ-SUKL) |
|---|---|
| | [Receiving Member State] |
| Procedure: | Mutual Recognition Procedure (MRP) |
| | [As the referral procedure remains non-centralised..] |
| Invented Name: | Proprietary-Wonderdrug |
| INN: | Ibuprofen |
| Sequence: | 4444 |
| | [The sequence number needs to be the next available sequence number within the product life cycle]. |
| Related Sequence: | |
| Submission Description: | Referral under Article 31 |

503
504
505
506 Example of the use of the submission type 'reformat'

507
508 The submission type 'reformat' should be used for each baseline submission. (Note: the submission type 'supplemental-info' should not be used for the
509 second reformat submission.) Related sequence should not be used.
510 An example is given below.

511

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

512
513
514

515 **Appendix 1.2: Country-Specific Elements**
516 A number of the elements that represent NtA Module 1 TOC headings possess the child element "specific", which allows country-specificity of content to be
517 explicitly indicated.

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

518  Module 1 elements that have "specific" child elements can therefore contain multiple documents, each with content for review by a different country. These
519  elements are listed below:
520    • `m1-0-cover`              (1.0 Cover Letter)
521    • `m1-2-form`               (1.2 Application Form)
522    • `m1-3-2-mockup`           (1.3.2 Mock-Up)
523    • `m1-3-3-specimen`         (1.3.3 Specimen)
524    • `m1-3-4-consultation`  (1.3.4 Consultation with Target Patient Groups)
525    • `m1-3-5-approved`         (1.3.5 Product Information Already Approved in the Member States)
526    • `m1-responses`           (Responses to Questions)
527    • `m1-additional-data`   (Additional Data)
528

529  **Appendix 1.3: Product Information Element Description**
530  The "`m1-3-1-spc-label-pl`" corresponds to the Notice to Applicants heading 1.3.1 SPC, Labelling and Package Leaflet. This element can have multiple
531  child "`pi-doc`" elements that allow identification of product information language, document type and applicable country as described below.

| Element | Attribute | Description/Instructions | Example | Constraint | Occurrence |
|---------|-----------|-------------------------|---------|------------|------------|
| pi-doc  |           | Parent element for identification of the type, language and country of one or more product information documents. | N/A | Mandatory | Repeatable |
|         | xml:lang  | The language that the product information is written in (see Appendix 2.2 for allowable values). | fr | Mandatory | Unique |
|         | type      | The type of product information document (see Appendix 2.3 for allowable values). | combined | Mandatory | Unique |
|         | country   | The receiving country for the product information (or "common") (see Appendix 2.1 for full list of allowable values) | be | Mandatory | Unique |

532

533

28

## Appendix 2: Directory / File Structure for Module 1

534

535
536 The directory / file structure is defined in this appendix as a table containing the following information:

537

| 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 |

538
539 Where the following conventions are used:

540

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

541

542
543 * = 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
544 for codes is for illustrative purposes only to show differentiation between the variable parts and the fixed part of the name.
545

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

| | | |
|---|---|---|
| 5 | Number | |
| | Title | |
| | Element | |
| | File | m1/eu/10-cover/*CC*/*CC*-cover-*VAR.EXT* |
| | Comment | Filename for the Cover Letter composed of a fixed component "*CC*", a fixed component "cover" and an optional variable component if required (e.g. fr-cover-variationrationale.pdf). When only the cover letter is submitted in this directory the file name should be *CC*-cover.pdf.<br>Single document correspondences e.g. Letter of Undertakings should be placed here. |
| 6 | Number | |
| | Title | |
| | Element | |
| | File | *m1/eu/10-cover/CC/CC-tracking-VAR.EXT* |
| | Comment | Note that the tracking table required with MPR/DCP submissions should be located within a 'common' directory, with the filename 'common-tracking-var.pdf'<br>In case of submissions of other procedure types the respective country code should be used, e.g. ema-tracking-var.pdf in case of a centralised procedure or de-tracking-var.pdf in case of a national procedure with BfArM or PEI. |
| 7 | 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). |
| 8 | Number | |
| | Title | |
| | Element | |
| | Directory | m1/eu/12-form/*CC* |
| | Comment | Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission. |
| 9 | Number | |
| | Title | |
| | Element | |

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

| 14 | Number | |
| --- | --- | --- |
| | Title | |
| | Element | |
| | File | m1/eu/13-pi/131-spclabelpl/*CC*/*LL*/*CC-PIDOC-VAR.EXT* |
| | Comment | Filename for the spc-label-pl document composed by a fixed component "*CC*", a fixed component "PIDOC" as per table of [Appendix 2.3](#) and an optional variable component to be used if needed (e.g. m1/eu/13-pi/131-spclabelpl/ema/de/ema-combined-tablet10mgde.pdf). |
| 15 | Number | 1.3.2 |
| | Title | Mock-up |
| | Element | m1-3-2-mockup |
| | Directory | m1/eu/13-pi/132-mockup |
| | Comment | |
| 16 | Number | |
| | Title | |
| | Element | |
| | Directory | m1/eu/13-pi/132-mockup/*CC* |
| | Comment | Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission. |
| 17 | Number | |
| | Title | |
| | Element | |
| | File | m1/eu/13-pi/132-mockup/*CC*/*CC*-mockup-*VAR.EXT* |
| | Comment | Filename for the mock-up document composed by a fixed component "*CC*", a fixed component "mockup" and an optional variable component to be used if needed. (e.g. fr-mockup-tablet10mgouter.pdf). |

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

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

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

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

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

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

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

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

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

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

| 68 | Number |  |
|---|---|---|
|  | Title |  |
|  | Element |  |
|  | File | m1/eu/responses/*CC*/*CC*-responses-*VAR.EXT* |
|  | Comment | Filename for responses to questions composed by a fixed component "*CC*", a fixed component "responses" and an optional variable component to be used if needed (e.g. be-responses.pdf). |
| 69 | Number |  |
|  | Title | Additional Data |
|  | Element | m1-additional-data |
|  | Directory | m1/eu/additional-data |
|  | Comment | The 'Additional Data' section should only be used for information required for National, MR and Decentralised Procedures; it is therefore not generally applicable for the Centralised Procedure, other than for justifications for active substances.. |
| 70 | Number |  |
|  | Title |  |
|  | Element |  |
|  | Directory | m1/eu/additional-data/*CC* |
|  | Comment | Always use the country directory at this level for all procedures even when only one file is submitted to only one country during the lifecycle of the submission. |
| 71 | Number |  |
|  | Title |  |
|  | Element |  |
|  | File | m1/eu/additional-data/*CC*/*CC*-additionaldata-*VAR.EXT* |
|  | Comment | Filename for additional information requested composed by a fixed component "*CC*", a fixed component "additionaldata" and an optional variable component to be used if needed (e.g. be-additionaldata-yellowpink.pdf). |
|  |  | Supporting data for variations should be not be placed in this section; wherever possible they should be placed in the relevant CTD section, primarily within Module 3 'Quality' and Module 1 (1.3.1) 'Summary of Product Characteristics, Labelling and Package Leaflet'. Where documents cannot be assigned to specific CTD-defined locations, then they should be attached to the 1.2 Application Form. The same approach should be used for renewals. Additionally see comments in row no 9. |
|  |  | The 'Additional Data' section should only be used for information required for country specific information/documentation for National, MR and Decentralised Procedures; it is not applicable for the Centralised Procedure, other than for justifications for active substances. |

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

546

**Appendix 2.1: Destination Codes**

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

550

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

551

552

**Appendix 2.2: Language Codes**

554

| Code | Language |
|------|----------|
| bg | Bulgarian |
| cs | Czech |
| da | Danish |
| de | German |
| el | Greek |
| en | English |
| es | Spanish |
| et | Estonian |
| fi | Finnish |
| fr | French |
| hr | Croatian |
| 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 |

555

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

557

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

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

559 **Appendix 2.4: Agency Codes and Names**

560

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

563
564

| Country | Agency Code | Human/Vet (H/V)* | Agency Name |
|---|---|---|---|
| Austria | AT-BASG | H/V | Austria - BASG-Austrian Federal Office for Safety in Health Care / Austrian Medicines and Medical Devices Agency |
| Belgium | BE-FAMHP | H/V | Belgium - Agence Fédérale des Médicaments et des Produits de Santé |
| Bulgaria | BG-BDA | H | Bulgaria - Bulgarian Drug Agency |
| Croatia | HR-HALMED | H | Croatia – Agency for Medicinal Products and Medical Devices of Croatia |
| Cyprus | CY-PHS | H/V | Cyprus - Pharmaceutical Services, Ministry of Health |
| Czech Rep. | CZ-SUKL | H | Czech Rep - State Institute for Drug Control |
| Denmark | DK-DHMA | H/V | Denmark - Danish Health and Medicines Authority |
| Estonia | EE-SAM | H/V | Estonia - State Agency of Medicines |
| EU | EU-EDQM | H/V | EDQM – European Directorate for the Quality of Medicines & HealthCare |
| EU | EU-EMA | H/V | EMA - European Medicines Agency |
| Finland | FI-FIMEA | H/V | Finland - Finnish Medicines Agency |
| France | FR-ANSM | H | France - ANSM - Agence nationale de sécurité du médicament et des produits de santé |
| Germany | DE-BFARM | H | Germany - BfArM - Bundesinstitut für Arzneimittel und Medizinprodukte |
| | DE-PEI | H/V | Germany – PEI - Paul-Ehrlich Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel |
| Greece | EL-EOF | H/V | Greece - EOF - National Drug Organisation |
| Hungary | HU-OGYI | H | Hungary - National Institute of Pharmacy |
| Iceland | IS-IMCA | H/V | Iceland - Icelandic Medicines Control Agency |
| Ireland | IE- HPRA | H/V | Ireland - The Health Products Regulatory Authority |
| Italy | IT-AIFA | H | Italy - Agenzia Italiana del Farmaco |
| Latvia | LV-ZVA | H/V | Latvia - State Agency of Medicines |

| | | | |
|---|---|---|---|
| Liechtenstein | LI-LLV | H/V | Liechtenstein - Kontrollstelle für Arzneimittel beim Amt für Lebensmittelkontrolle und Veterinärwesen |
| Lithuania | LT-SMCA | H | Lithuania - State Medicines Control Agency |
| Luxembourg | LU-MINSANT | H/V | Luxembourg - Direction de la Santé Villa Louvigny Division de la Pharmacie et des Medicaments |
| Malta | MT-MEDAUTH | H | Malta - Medicines Authority Divizjoni Tas-Sahha Bezzjoni Ghar-Regolazzjoni Tal-Medicini |
| Netherlands | NL-MEB | H/V | Netherlands - College ter Beoordeling van Geneesmiddelen Medicines Evaluation Board |
| Norway | NO-NOMA | H/V | Norway - The Norwegian Medicines Agency |
| Poland | PL-URPL | H/V | Poland - Office for Registration of Medicinal Products, Medical Devices and Biocidal Products |
| Portugal | PT-INFARMED | H/V | Portugal - INFARMED - Instituto Nacional da Farmácia e do Medicamento Parque da Saúde de Lisboa |
| Romania | RO-ANMMD | H/V | Romania- National Agency for Medicines and Medical Devices |
| Slovak Rep. | SK-SIDC | H | Slovak Rep - State Institute for Drug Control |
| Slovenia | SI-JAZMP | H/V | Slovenia - Javna agencija Republike Slovenije za zdravila in medicinske pripomočke |
| Spain | ES-AEMPS | H/V | Spain - Agencia Española de Medicamentos y Productos Sanitarios |
| Sweden | SE-MPA | H/V | Sweden - Medical Products Agency |
| United Kingdom | UK-MHRA | H | Medicines and Healthcare products Regulatory Agency |

565
566
567  *eCTD apply only for Marketing Authorisation applications for medicinal products for human use.
568

569

## Appendix 3: Modularised DTD for EU Module 1

**571** **eu-regional.dtd**

572

```
573  <!--
574  PUBLIC "-//EU//DTD eCTD EU Backbone 3.0//EN"
575  In the eCTD File Organisation: "util/dtd/eu-regional.dtd"
576
577  August 2009
578
579  Contributors:
580      ANSM (Aziz Diop)
581      EMA (Laurent Desqueper)
582      MEB (C.A. van Belkum)
583
584  February 2013
585
586  Contributors:
587        EMA (Antonios Yfantis)
588
589  June 2015
590
591  Contributors:
592        BFARM (Klaus Menges)
593
594  Meaning or value of the  suffixes:
595      ?  : element must appear 0 or 1 time
596      *  : element must appear 0 or more time
597      +  : element must appear 1 or more times
598      <none>: element must appear once and only once
599  -->
600
601  <!-- General declarations, external modules
602  references.................. -->
603  <!ENTITY % countries
604  "(at|be|bg|common|cy|cz|de|dk|edqm|ee|el|es|ema|fi|fr|hr|hu|ie|is|it
605  |li|lt|lu|lv|mt|nl|no|pl|pt|ro|se|si|sk|uk)">
606  <!ENTITY % languages
607  "(bg|cs|da|de|el|en|es|et|fi|fr|hr|hu|is|it|lt|lv|mt|nl|no|pl|pt|ro|
608  sk|sl|sv)">
609
610  <!ENTITY % leaf-node "(( leaf | node-extension )*)">
611
612  <!ENTITY % envelope-module SYSTEM "eu-envelope.mod" >
613  %envelope-module;
614
615  <!ENTITY % leaf-module SYSTEM "eu-leaf.mod" >
616  %leaf-module;
617
618  <!ELEMENT specific (
619      %leaf-node;
620  )>
621  <!ATTLIST specific
622      country %countries; #REQUIRED
623  >
624  <!ELEMENT pi-doc (
625      %leaf-node;
```

```
626    )>
627    <!ATTLIST pi-doc
628        xml:lang %languages; #REQUIRED
629        type      (spc|annex2|outer|interpack|impack|other|pl|combined)
630    #REQUIRED
631        country  %countries;    #REQUIRED
632    >
633
634    <!-- Root element
635    .............................................. -->
636    <!ELEMENT eu:eu-backbone (
637        eu-envelope,
638        m1-eu
639    )>
640
641    <!ATTLIST eu:eu-backbone
642        xmlns:eu        CDATA #FIXED   "http://europa.eu.int"
643        xmlns:xlink     CDATA #FIXED   "http://www.w3c.org/1999/xlink"
644        xml:lang        CDATA #IMPLIED
645        dtd-version     CDATA #FIXED   "3.0"
646    >
647
648    <!--
649    ...........................................................................
650    -->
651    <!ELEMENT m1-eu (
652        m1-0-cover,
653        m1-2-form?,
654        m1-3-pi?,
655        m1-4-expert?,
656        m1-5-specific?,
657        m1-6-environrisk?,
658        m1-7-orphan?,
659        m1-8-pharmacovigilance?,
660        m1-9-clinical-trials?,
661        m1-10-paediatrics?,
662        m1-responses?,
663        m1-additional-data?
664    )>
665
666    <!--
667    ...........................................................................
668    -->
669    <!ELEMENT m1-0-cover (
670        specific+
671    )>
672
673    <!--
674    ...........................................................................
675    -->
676    <!ELEMENT m1-2-form (
677        specific+
678    )>
679
```

```
680   <!--
681   ........................................................................
682   -->
683   <!ELEMENT m1-3-pi (
684       m1-3-1-spc-label-pl?,
685       m1-3-2-mockup?,
686       m1-3-3-specimen?,
687       m1-3-4-consultation?,
688       m1-3-5-approved?,
689       m1-3-6-braille?
690   )>
691
692   <!ELEMENT m1-3-1-spc-label-pl (
693       pi-doc+
694   )>
695
696   <!ELEMENT m1-3-2-mockup (
697       specific+
698   )>
699   <!ELEMENT m1-3-3-specimen (
700       specific+
701   )>
702   <!ELEMENT m1-3-4-consultation (
703       specific+
704   )>
705   <!ELEMENT m1-3-5-approved (
706       specific+
707   )>
708   <!ELEMENT m1-3-6-braille (
709       %leaf-node;
710   )>
711
712   <!--
713   ........................................................................
714   -->
715   <!ELEMENT m1-4-expert (
716       m1-4-1-quality?,
717       m1-4-2-non-clinical?,
718       m1-4-3-clinical?
719   )>
720
721   <!ELEMENT   m1-4-1-quality         %leaf-node;>
722   <!ELEMENT   m1-4-2-non-clinical    %leaf-node;>
723   <!ELEMENT   m1-4-3-clinical        %leaf-node;>
724
725   <!--
726   ........................................................................
727   -->
728   <!ELEMENT m1-5-specific (
729       m1-5-1-bibliographic?,
730       m1-5-2-generic-hybrid-bio-similar?,
731       m1-5-3-data-market-exclusivity?,
732       m1-5-4-exceptional-circumstances?,
733       m1-5-5-conditional-ma?
734   )>
735
```

```
736   <!ELEMENT m1-5-1-bibliographic                          %leaf-node;>
737   <!ELEMENT m1-5-2-generic-hybrid-bio-similar          %leaf-node;>
738   <!ELEMENT m1-5-3-data-market-exclusivity               %leaf-
739   node;>
740   <!ELEMENT m1-5-4-exceptional-circumstances        %leaf-node;>
741   <!ELEMENT m1-5-5-conditional-ma  %leaf-node;>
742
743   <!--
744   ...........................................................................
745   -->
746   <!ELEMENT m1-6-environrisk (
747       (m1-6-1-non-gmo | m1-6-2-gmo)?
748   )>
749   <!ELEMENT   m1-6-1-non-gmo    %leaf-node;>
750   <!ELEMENT   m1-6-2-gmo        %leaf-node;>
751
752   <!--
753   ...........................................................................
754   -->
755   <!ELEMENT m1-7-orphan (
756       m1-7-1-similarity?,
757       m1-7-2-market-exclusivity?
758   )>
759   <!ELEMENT   m1-7-1-similarity    %leaf-node;>
760   <!ELEMENT   m1-7-2-market-exclusivity   %leaf-node;>
761
762   <!--
763   ...........................................................................
764   -->
765   <!ELEMENT m1-8-pharmacovigilance (
766       m1-8-1-pharmacovigilance-system?,
767       m1-8-2-risk-management-system?
768   )>
769   <!ELEMENT   m1-8-1-pharmacovigilance-system  %leaf-node;>
770   <!ELEMENT   m1-8-2-risk-management-system    %leaf-node;>
771
772   <!--
773   ...........................................................................
774   -->
775   <!ELEMENT m1-9-clinical-trials   %leaf-node;>
776
777   <!--
778   ...........................................................................
779   -->
780   <!ELEMENT m1-10-paediatrics     %leaf-node;>
781
782   <!--
783   ...........................................................................
784   -->
785   <!ELEMENT m1-responses (
786       specific+
787   )>
788
789   <!--
790   ...........................................................................
791   -->
```

```
792  <!ELEMENT m1-additional-data (
793     specific+
794  )>
```

**795**    **eu-envelope.mod**

**796**

```
797   <!--
798   In the eCTD File Organisation: "util/dtd/eu-envelope.mod"
799
800   Version 1.4
801
802   February 2009
803
804   Contributors:
805      ANSM (Aziz Diop)
806      EMA (Laurent Desqueper)
807      MEB (C.A. van Belkum)
808
809   Version 2.0
810   February 2013
811
812   Contributors:
813        EMA (Antonios Yfantis)
814
815   Version 3.0
816   July 2015
817
818   Contributors:
819        BFARM (Klaus Menges)
820
821   -->
822
823   <!--
824   .....................................................................
825   -->
826   <!ELEMENT eu-envelope (
827        envelope+
828   )>
829
830   <!ELEMENT envelope (
831        identifier,
832        submission,
833        submission-unit,
834        applicant,
835        agency,
836        procedure,
837        invented-name+,
838        inn*,
839        sequence,
840        related-sequence*,
841        submission-description
842   )>
843
844   <!--
845   .....................................................................
846   -->
847   <!ELEMENT identifier            ( #PCDATA )  >
848   <!ELEMENT submission            ( number?, procedure tracking )  >
849   <!ELEMENT procedure tracking        ( number+ )>
```

```
850  <!ELEMENT number                ( #PCDATA )>
851  <!ELEMENT submission-unit       ( #PCDATA )>
852  <!ELEMENT applicant             ( #PCDATA )>
853  <!ELEMENT agency                EMPTY>
854  <!ELEMENT procedure             EMPTY  >
855  <!ELEMENT invented-name    ( #PCDATA )>
856  <!ELEMENT inn                   ( #PCDATA )>
857  <!ELEMENT sequence              ( #PCDATA )>
858  <!ELEMENT related-sequence ( #PCDATA )>
859  <!ELEMENT submission-description    ( #PCDATA )>
860
861  <!--
862  ....................................................................
863  -->
864  <!ATTLIST submission
865   type (maa | var-type1a | var-type1ain | var-type1b | var-type2 |
866  var-nat | extension | psur | psusa | rmp | renewal | pam-sob | pam-
867  anx | pam-mea | pam-leg | pam-sda | pam-cada | pam-p45 | pam-p46 |
868  pam-paes | pam-rec | pass107n | pass107q | asmf | pmf | referral-20
869  | referral-294 | referral-29p | referral-30 | referral-31 |
870  referral-35 | referral-53 | referral-107i | referral-16c1c |
871  referral-16c4 | annual-reassessment | usr | clin-data-pub-rp | clin-
872  data-pub-fv | paed-7-8-30 | paed-29 | paed-45 | paed-46 | article-58
873  | notification-61-3 | transfer-ma | lifting-suspension | withdrawal
874  | cep | none) #REQUIRED
875   mode ( single | grouping | worksharing ) #IMPLIED
876  >
877
878  <!ATTLIST submission-unit
879   type (initial | validation-response | response | additional-info |
880  closing | consolidating | corrigendum | reformat ) #REQUIRED
881  >
882
883  <!--
884  ....................................................................
885  -->
886  <!ATTLIST agency
887  code ( AT-BASG | BE-FAMHP | BG-BDA | CY-PHS | CZ-SUKL | DE-BFARM |
888  DE-PEI | DK-DHMA | EE-SAM | EL-EOF | ES-AEMPS | FI-FIMEA | FR-ANSM |
889  HR-HALMED | HU-OGYI | IE-HPRA | IS-IMCA | IT-AIFA | LI-LLV | LT-SMCA
890  | LU-MINSANT | LV-ZVA | MT-MEDAUTH | NL-MEB | NO-NOMA | PL-URPL |
891  PT-INFARMED | RO-ANMMD | SE-MPA | SI-JAZMP | SK-SIDC | UK-MHRA | EU-
892  EMA | EU-EDQM ) #REQUIRED>
893
894  <!--
895  ....................................................................
896  -->
897  <!ATTLIST procedure
898   type (
899     centralised
900   | national
901   | mutual-recognition
902   | decentralised
903   ) #REQUIRED
904  >
905
```

```
906    <!--
907    ....................................................................
908    -->
909    <!ENTITY % env-countries
910    "(at|be|bg|cy|cz|de|dk|edqm|ee|el|ema|es|fi|fr|hr|hu|ie|is|it|li|lt|
911    lu|lv|mt|nl|no|pl|pt|ro|se|si|sk|uk)">
912
913    <!--
914    ....................................................................
915    -->
916    <!ATTLIST envelope country %env-countries; #REQUIRED >
917
918    <!-- +++ -->
```

919 **eu-leaf.mod**

920

```
921  <!--
922  In the eCTD File Organisation: "util/dtd/eu-leaf.mod"
923
924  Version 1.4
925  August 2009
926
927  Contributors:
928      ANSM (Aziz Diop)
929      EMA (Laurent Desqueper)
930      MEB (C.A. van Belkum)
931
932  This is based on ich-ectd-3-2.dtd;
933
934  If the ich-ectd.dtd is modularized, this one could be replaced.
935  Hence, one is certain that the common and EU leaf are the same.
936  -->
937
938  <!-- ================================================================ -
939  ->
940  <!ELEMENT node-extension (title, (leaf | node-extension)+)>
941  <!ATTLIST node-extension
942        ID ID #IMPLIED
943        xml:lang CDATA #IMPLIED
944  >
945
946  <!-- ================================================================ -
947  ->
948  <!ENTITY % show-list " (new | replace | embed | other | none) ">
949  <!ENTITY % actuate-list " (onLoad | onRequest | other | none) ">
950  <!ENTITY % operation-list " (new | append | replace | delete) ">
951  <!ENTITY % leaf-element " (title, link-text?) ">
952  <!ENTITY % leaf-att '
953   ID                   ID                   #REQUIRED
954   application-version CDATA                 #IMPLIED
955   version              CDATA                #IMPLIED
956   font-library         CDATA                #IMPLIED
957   operation           %operation-list;    #REQUIRED
958   modified-file        CDATA                #IMPLIED
959   checksum             CDATA                #REQUIRED
960   checksum-type        CDATA                #REQUIRED
961   keywords             CDATA                #IMPLIED
962   xmlns:xlink          CDATA                #FIXED
963  "http://www.w3c.org/1999/xlink"
964   xlink:type           CDATA                #FIXED     "simple"
965   xlink:role           CDATA                #IMPLIED
966   xlink:href           CDATA                #IMPLIED
967   xlink:show          %show-list;          #IMPLIED
968   xlink:actuate       %actuate-list;       #IMPLIED
969   xml:lang             CDATA                #IMPLIED
970   '>
971
972  <!ELEMENT leaf %leaf-element;>
973  <!ATTLIST leaf
```

```
974        %leaf-att;
975    >
976    <!ELEMENT title (#PCDATA)>
977    <!ELEMENT link-text (#PCDATA | xref)*>
978
979    <!ELEMENT xref EMPTY>
980    <!ATTLIST xref
981        ID ID #REQUIRED
982        xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
983        xlink:type CDATA #FIXED "simple"
984        xlink:role CDATA #IMPLIED
985        xlink:title CDATA #REQUIRED
986        xlink:href CDATA #REQUIRED
987        xlink:show %show-list; #IMPLIED
988        xlink:actuate %actuate-list; #IMPLIED
989    >
990
991    <!-- +++ -->
992
```