# EU Module 1 Specification - Annex
## Version 1.4.1

## November 2011

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| 0.4 | November, 2001 | Stan van Belkum | Draft |
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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 |
| 0.91 | EU Regulators ICH, EMEA | EU Regulatory Authorities, EMEA |
| 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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| 1.2 | | |
| 1.2.1 | | |
| 1.3 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, Pharma, other interested parties |
| 1.4 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, EGA, other interested parties |
| 1.4.1 | EU Regulators, interested parties | EU Regulatory Authorities (members TIGes and NtA), EFPIA, EGA, other interested parties |

*Distribution*

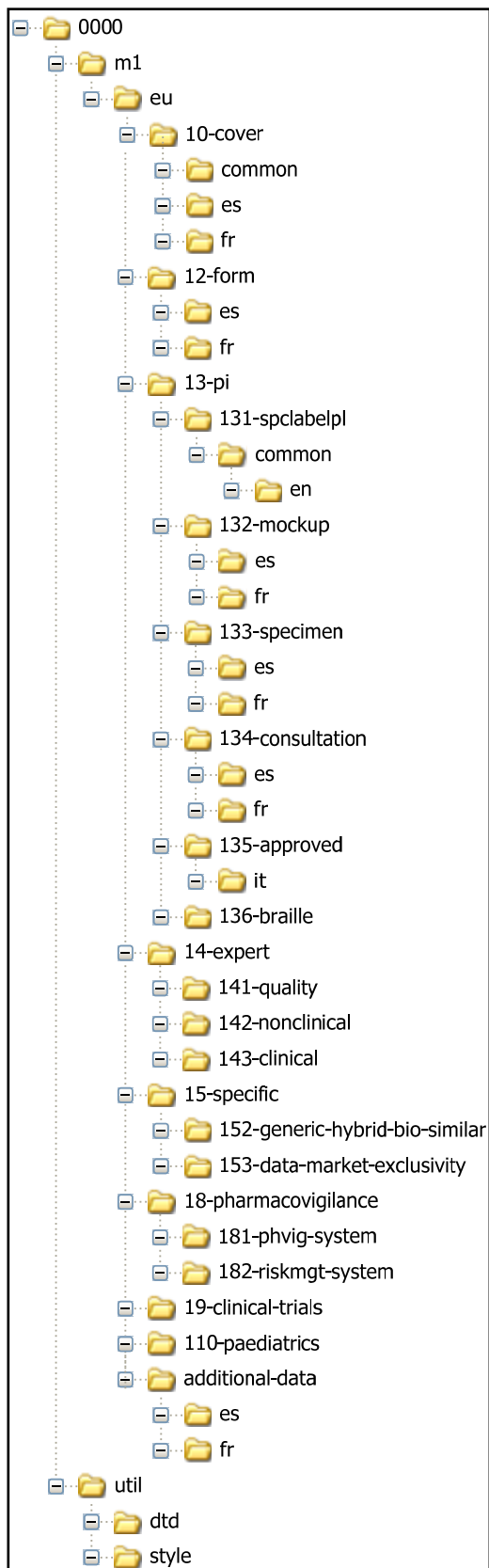| Version | Name | Organisation |
|---------|------|--------------|
| 0.4 | http://esubmission.eudra.org | |
| 0.7 | http://esubmission.eudra.org | |
| 0.8 | http://esubmission.eudra.org | |
| 0.91 | | |
| 0.92 | http://esubmission.eudra.org | |
| 0.95.1 | http://esubmission.eudra.org | |
| 0.95.2 | http://esubmission.eudra.org | |
| 0.95.3 | http://esubmission.eudra.org | |
| 1.0 | http://pharmacos.eudra.org/F2/eudralex/vol-2/home.htm | |
| 1.1 | | |
| 1.2 | | |
| 1.2.1 | http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm | |
| 1.3 | http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm | |
| 1.4 | http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm | |
| 1.4.1 | http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm | |

# TABLE OF CONTENT

# Annex 1: Directory Structure Examples

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

## MRP Directory Structure

```
0000
  m1
    eu
      10-cover
        common
        es
        fr
      12-form
        es
        fr
      13-pi
        131-spclabelpl
          common
            en
        132-mockup
          es
          fr
        133-specimen
          es
          fr
        134-consultation
          es
          fr
        135-approved
          it
        136-braille
      14-expert
        141-quality
        142-nonclinical
        143-clinical
      15-specific
        152-generic-hybrid-bio-similar
        153-data-market-exclusivity
      18-pharmacovigilance
        181-phvig-system
        182-riskmgt-system
      19-clinical-trials
      110-paediatrics
      additional-data
        es
        fr
    util
      dtd
      style
```
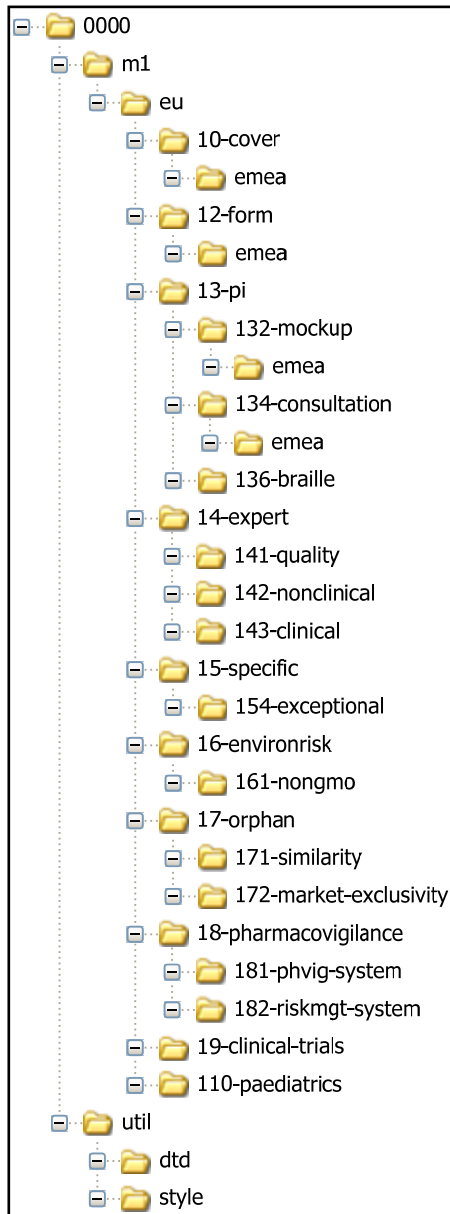
.

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

This example is provided with the following options:
- Italy as RMS,
- France and Spain as CMSs,
- Submission of PI in PDF - note that this is the initial submission of the basic text in English
- generic, hybrid or bio-similar application

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## Centralised Procedure Directory Structure

```
0000
  m1
    eu
      10-cover
        emea
      12-form
        emea
      13-pi
        132-mockup
          emea
        134-consultation
          emea
        136-braille
      14-expert
        141-quality
        142-nonclinical
        143-clinical
      15-specific
        154-exceptional
      16-environrisk
        161-nongmo
      17-orphan
        171-similarity
        172-market-exclusivity
      18-pharmacovigilance
        181-phvig-system
        182-riskmgt-system
      19-clinical-trials
      110-paediatrics
  util
    dtd
    style
```
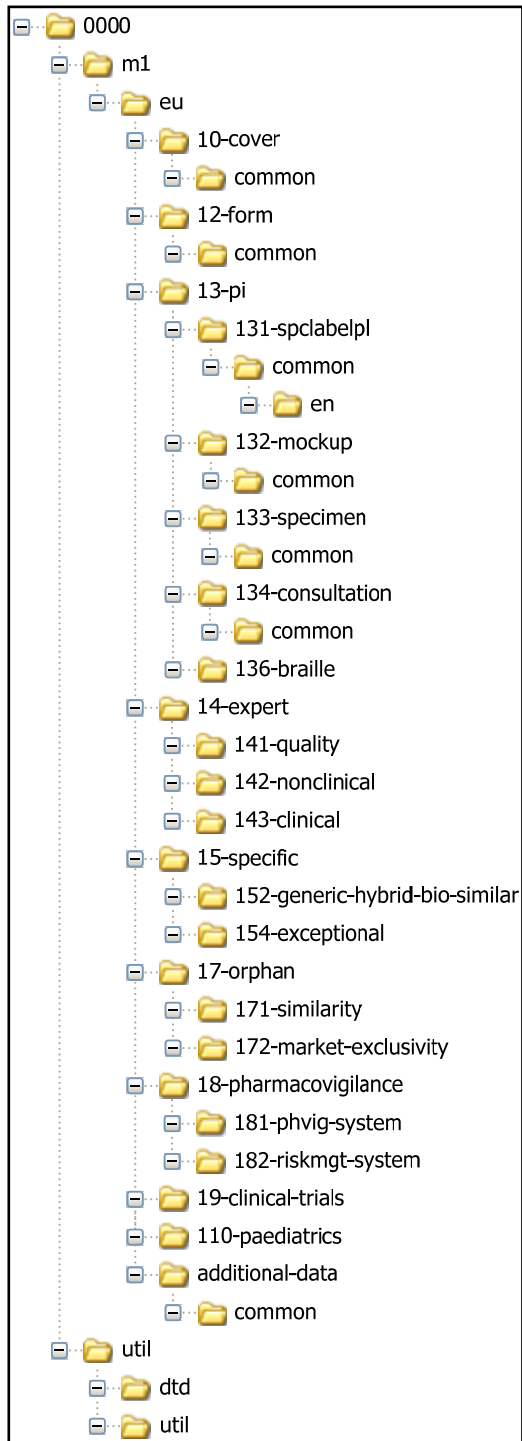
For the Centralised Procedure, most documents will be in English and valid for all European countries. Files should be placed in the country directories inside the 'emea' directory (for instance cf. directory "10-cover").

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

Note: the Additional Data section should not be used in a Centralised Procedure submission.
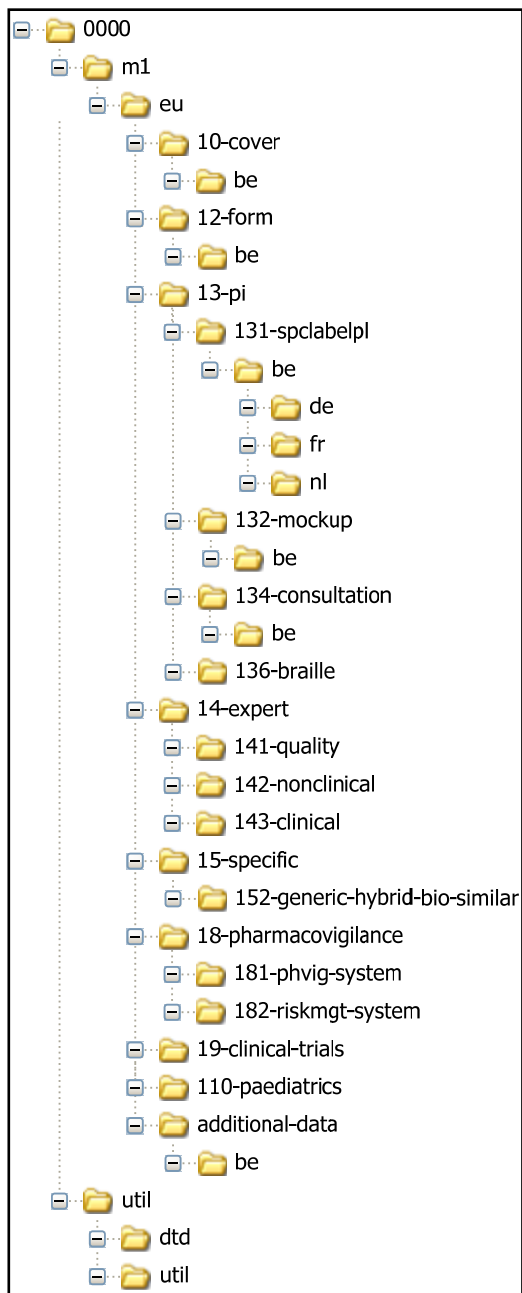
## Decentralised Procedure Directory Structure

```
0000
  m1
    eu
      10-cover
        common
      12-form
        common
      13-pi
        131-spclabelpl
          common
            en
        132-mockup
          common
        133-specimen
          common
        134-consultation
          common
        136-braille
      14-expert
        141-quality
        142-nonclinical
        143-clinical
      15-specific
        152-generic-hybrid-bio-similar
        154-exceptional
      17-orphan
        171-similarity
        172-market-exclusivity
      18-pharmacovigilance
        181-phvig-system
        182-riskmgt-system
      19-clinical-trials
      110-paediatrics
      additional-data
        common
  util
    dtd
    util
```

For the Decentralised Procedure during the mutual phases, most documents will be in English and valid for all European countries. As a result, most files should be placed in the common folder. No country or language folder should be added. However, some exceptions may remain during the mutual phase, such as the submission of country specific additional requirements.

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

National Procedure Directory Structure

```
0000
  m1
    eu
      10-cover
        be
      12-form
        be
      13-pi
        131-spclabelpl
          be
            de
            fr
            nl
        132-mockup
          be
        134-consultation
          be
        136-braille
      14-expert
        141-quality
        142-nonclinical
        143-clinical
      15-specific
        152-generic-hybrid-bio-similar
      18-pharmacovigilance
        181-phvig-system
        182-riskmgt-system
      19-clinical-trials
      110-paediatrics
      additional-data
        be
  util
    dtd
    util
```

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

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

This example is provided with the following options:
- Belgium as the country for the submission
- Product Information documents provided in all three official languages of Belgium

**General Notes:**

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

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

## Annex 2: Creating the XML EU Regional Submission

The name to be used as the directory name in the top-level directory is to be decided by the applicant, as the agency tracking number[1] is not always known in advance and so cannot be used.

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

Each submission should be differentiated by a sub-directory named according to the sequence number of the submission to the EU regulatory agency. The agency tracking number (if available) and sequence number should be included in the "`eu-envelope`" element of the EU Regional instance. The first sub-directory below the top-level directory for the original submission should have the sequence number "0000" and e.g. the three subsequent submissions respectively "0001", "0002" and "0003".

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

1. Select a tag element that best corresponds to the document or file being submitted. For example, select the tag `<m1-0-cover>` to submit a file containing the cover letter for the submission.
   N.B. The operator used for the cover letter should always be "`new`".
   Create a child `<specific>` element for the `<m1-0-cover>` tag to identify for which country the cover letter is intended. The country information is stored in the attribute "`country`". When a file applies to all countries in the Centralised Procedure, it is recommended to use the "`emea`" country. In the case of Decentralised Procedure, it is recommended to use the "`common`" country if this is a sequence as part of the mutual phase, otherwise you may need to add country specific cover letters.

2. Create a child `<leaf>` element for the `<specific>` tag created above. If more than one file belongs at this level (and country), you may create more than one `<leaf>` element under the tag.

3. Provide the relative location compared to the location of the `eu-regional.xml` file and file name of the actual file containing the cover letter using the "`xlink:href`" attribute for the `<leaf>` element (e.g. `xlink:href="10-cover/emea/emea-cover.pdf"`)

4. Provide a descriptive title for the file using the `<title>` element of the `<leaf>` element.

5. Provide information for the appropriate attributes of the `<leaf>` element as described in Appendix 2 of the ICH eCTD specification.

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

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[1] 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 an MRP/DCP number (e.g. DE/H/0126/001/MR), a national procedure number (e.g. 2131577), the EMEA application number (e.g. EMEA/H/C/000123 or EMEA/H/C/000123/II/13), an authorisation or licence number (e.g. EU/1/00/44/0003 – 0004), any other number used by an agency to track a submission (e.g. PL01234/0003-0004), or a number used by the applicant to manage the submission within their company (e.g. Pharmacompany123). There must be at least one tracking number identified from the regulators and, in addition, the applicant can choose to include an internal tracking number. It is suggested that if the procedure number has not yet been allocated by the agency then the term 'to be advised' should be used. Applicants should consult national guidance for further information.

## Instructions for a Simple New Submission

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

```xml
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "..\..\util\dtd\eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="..\..\util\style\eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
   xmlns:xlink="http://www.w3c.org/1999/xlink" dtd-version="1.4">
   <eu-envelope>
      <envelope country="emea">
         <submission type="initial-maa">
            <tracking>
               <number>to be advised</number>
            </tracking>
         </submission>
         <applicant>Pharma Unlimited</applicant>
         <agency code="EU-EMEA"/>
         <procedure type="centralised"/>
         <invented-name>WonderPill</invented-name>
         <inn>INN-PIL</inn>
         <sequence>0000</sequence>
         <submission-description>Initial submission</submission-description>
      </envelope>
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         <specific country="emea">
            <leaf ID="id-cover-1" operation="new"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="10-cover/emea/emea-cover.pdf">
               <title>Cover Letter for EMEA</title>
            </leaf>
         </specific>
      </m1-0-cover>
      <m1-2-form>
         <specific country="emea">
            <leaf ID="id-form-1" operation="new"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="12-form/emea/emea-form.pdf">
               <title>Application Form</title>
            </leaf>
         </specific>
      </m1-2-form>
   </m1-eu>
</eu:eu-backbone>
```

## Instructions for Submission of Supplemental Information

In this example, a replacement application form is submitted.

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

```xml
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "..\..\util\dtd\eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="..\..\util\style\eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
   xmlns:xlink="http://www.w3c.org/1999/xlink" dtd-version="1.4">
   <eu-envelope>
      <envelope country="emea">
         <submission type="supplemental-info">
            <tracking>
               <number>EMEA/H/C/000456</number>
            </tracking>
         </submission>
         <applicant>Pharma Unlimited</applicant>
         <agency code="EU-EMEA"/>
         <procedure type="centralised"/>
         <invented-name>WonderPill</invented-name>
         <inn>INN-PIL</inn>
         <sequence>0012</sequence>
         <related-sequence>0011</related-sequence>
         <submission-description>Final amended translations</submission-description>
      </envelope>
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         <specific country="emea">
            <leaf ID="id-cover-1" operation="new"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="10-cover/emea/emea-cover.pdf">
               <title>Cover Letter for EMEA</title>
            </leaf>
         </specific>
      </m1-0-cover>
      <m1-2-form>
         <specific country="emea">
            <leaf ID="id-form-2" operation="replace"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="12-form/emea/emea-form.pdf"
               modified-file="../../../0000/m1/eu/eu-regional.xml# id-form-1">
               <title>Revised Application Form</title>
            </leaf>
         </specific>
      </m1-2-form>
</m1-eu>
</eu:eu-backbone>
```

## Instructions for MRP and DCP Submissions

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

```xml
<?xml version="1.0" encoding="UTF-8"?>
<!DOCTYPE eu:eu-backbone SYSTEM "..\..\util\dtd\eu-regional.dtd">
<?xml-stylesheet type="text/xsl" href="..\..\util\style\eu-regional.xsl"?>
<eu:eu-backbone xmlns:eu="http://europa.eu.int"
   xmlns:xlink="http://www.w3c.org/1999/xlink" dtd-version="1.4">
   <eu-envelope>
      <envelope country="es">
         <submission type="supplemental-info" mode="single">
            <tracking>
               <number>ES/H/0123/001/II/987</number>
            </tracking>
         </submission>
         <applicant>PharmaCompany</applicant>
         <agency code="ES-AGEMED"/>
         <procedure type="mutual-recognition"/>
         <invented-name>WonderPill</invented-name>
         <inn>Pioglitazone hydrochloride</inn>
         <sequence>0012</sequence>
         <related-sequence>0011</related-sequence>
         <submission-description>Amendment SPC 4.8 after 4th PSUR</submission-
description>
      </envelope>
      <envelope country="fr">
         <submission type="supplemental-info" mode="single">
            <tracking>
               <number>ES/H/0123/001/II/987</number>
            </tracking>
         </submission>
         <applicant>PharmaCompany</applicant>
         <agency code="FR-AFSSAPS"/>
         <procedure type="mutual-recognition"/>
         <invented-name>WonderPill</invented-name>
         <inn>Pioglitazone hydrochloride</inn>
         <sequence>0012</sequence>
         <related-sequence>0011</related-sequence>
         <submission-description>Amendment SPC 4.8 after 4th PSUR</submission-
description>
      </envelope>
   </eu-envelope>
   <m1-eu>
      <m1-0-cover>
         <specific country="common">
            <leaf ID="cover-common" operation="new"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="10-cover/common/common-cover.pdf">
               <title>Cover Letter</title>
            </leaf>
         </specific>
         <specific country="common">
            <leaf ID="tracking-common" operation="new"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="10-cover/common/common-cover-tracking.pdf">
               <title>Tracking table</title>
            </leaf>
         </specific>
      </m1-0-cover>
      <m1-2-form>
         <specific country="common">
            <leaf ID="form-common" operation="new"
               checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
               xlink:href="12-form/common/common-form.pdf">
```

```xml
                  <title>Application Form</title>
               </leaf>
            </specific>
         </m1-2-form>
         <m1-3-pi>
            <m1-3-1-spc-label-pl>
               <pi-doc xml:lang="en" type="spc" country="common">
                  <leaf ID="spc-en" operation="replace"
                     checksum="d026431303be07099618458b24f8d8a9" checksum-type="md5"
                     xlink:href="13-pi/131-spclabelpl/common/en/uk-spc.pdf"
                     modified-file="../../../0011/m1/eu/eu-regional.xml#spc-en">
                     <title>SPC in English</title>
                  </leaf>
               </pi-doc>
            </m1-3-1-spc-label-pl>
         </m1-3-pi>
      </m1-eu>
</eu:eu-backbone>
```

## Annex 3: Envelopes for Different Submission Modes (Variations / Extensions)

This annex describes the usage of the "submission" field in the envelope for the cases of variations and extension applications. The EU Module 1 foresees the following modes:
- 'Single' (variation)
- 'Grouping' (variations of the same type affecting the same marketing authorisation)
- 'Grouping' (variations of different types affecting the same marketing authorisation)
- 'Grouping' (one or more Type IA variations affecting multiple marketing authorisations of the same MAH – a high level submission number is also required for these submissions)
- 'Worksharing' (one or more Type IB and/or Type II variation(s) affecting multiple marketing authorisations of the same MAH – a high level submission number is also required for these submissions)

### *Single Variation*

When submitting an eCTD for a single variation, the "submission" field in the envelope needs to be set to the mode "single". The submission type is for instance set to 'var-type1a'. The procedure number is unique, and is provided within the "number" field below the "tracking" element.

The example below describes the submission of a single variation of Type IA under the Centralised Procedure (assuming that 44 variations have already been submitted up to the point of example – this principle of providing an example from mid-lifecycle of the product applies to all variation numbers in all subsequent examples).

```
<envelope country="emea">
   <submission type="var-type1a" mode="single">
     <tracking>
        <number>EMEA/H/C/000123/IA/045</number>
     </tracking>
   </submission>
   …
</envelope>
```

### *Grouping of Variations of the Same Type, for a single MA*

When submitting an eCTD for multiple variations of the same type (e.g. Type 1B), the "submission" field in the envelope needs to be set to the mode "grouping". The submission type is set to 'var-type1b'. No high-level number is applied. The procedure/tracking number is unique and should be the next sequential number for the product concerned with the addition of the suffix 'G'.
The example below describes the submission of a grouping of variations of Type IB under the Centralised Procedure.

```
<envelope country="emea">
   <submission type="var-type1b" mode="grouping">
     <tracking>
        <number>EMEA/H/C/000123/IB/046/G</number>
     </tracking>
   </submission>
   …
</envelope>
```

## Grouping of Variations of Different Types, for a single MA

When submitting an eCTD for multiple variations of different types (e.g. Type II and Type IB), the "submission" field in the envelope needs to be set to the mode "grouping". The submission type is set to the 'highest' variation type included in the group, namely: 'var-type2'. No high-level number is applied. The procedure/tracking number is unique and should be the next sequential number for the product concerned with the addition of the suffix 'G'. Note that if, during the conduct of the process, a variation is withdrawn, the procedure type will not be amended. A consolidation sequence should always be sent at the end of the procedure, reflecting the approved scope of the variation. See guidance for further details.

The example below describes the submission of a grouping of variations of Type IB and Type II under the Centralised Procedure.

```
<envelope country="emea">
  <submission type="var-type2" mode="grouping">
    <tracking>
      <number>EMEA/H/C/000123/II/047/G</number>
    </tracking>
  </submission>
  …
</envelope>
```

## Grouping of Type IA Variation(s), for multiple MAs

When submitting an eCTD for one or more Type IA variations for more than one MA of the same MAH, the "submission" field in the envelope needs to be set to the mode "grouping". The submission type is set to 'var-type1a'.

The submission needs to have a high-level submission number that encompasses all marketing authorisations impacted by the submission. The high-level number needs to be provided below the "submission" field, within a dedicated "number" element. (The specific term to be used for this high-level number, as well as its abbreviation, is still under discussion. For the purposes of this document, the term 'IG' is used, although this may be subject to change in the future).

In addition, for each affected marketing authorisation, a tracking number needs to be provided within the "number" field below the "tracking" element.

Note that for each affected marketing authorisation, a separate eCTD submission must be provided. The high-level number will be the same for each of the separate eCTD submissions.

The examples below describe the submission of a grouping of Type IA variations under the Centralised Procedure, for 2 marketing authorisations (procedure numbers 000123 and 000456).

```
<envelope country="emea">
  <submission type="var-type1a" mode="grouping">
    <number>EMEA/H/XXXX/IG/002</number>
    <tracking>
      <number>EMEA/H/C/000123/IG002</number>
    </tracking>
  </submission>
  …
</envelope>
```

```
<envelope country="emea">
  <submission type="var-type1a" mode="grouping">
    <number>EMEA/H/XXXX/IG/002</number>
    <tracking>
      <number>EMEA/H/C/000456/IG002</number>
    </tracking>
  </submission>
  …
</envelope>
```

Note that the high-level number is assigned by the EMEA/regulatory agency/regulatory tracking system, and therefore might not be known by the applicant/MAH for the first submission. In such cases, the relevant part of the value should be populated as "xxxx". Once defined by the Agency, the high-level number should be used in the subsequent submissions.


## *Worksharing – Type IB and/or Type II Variations, for multiple MAs*

When submitting an eCTD for worksharing, the "submission" field in the envelope needs to be set to the mode "worksharing". The submission type is for instance set to the 'highest' variation type included in the group (e.g. 'var-type2' when grouping Type IB and Type II variations).

The submission needs to have a high-level 'worksharing' number that encompasses the full set of variations/marketing authorisations impacted by the submission. The 'worksharing' number needs to be provided below the "submission" field, within a dedicated "number" element.

In addition, for each affected marketing authorisation, a tracking number needs to be provided within the "number" field below the "tracking" element.

Note that for each affected marketing authorisation, a separate eCTD submission must be provided. The high-level worksharing number will be the same for each of the separate eCTD submissions, but the tracking number provided in addition will only refer to the MA in question.

The examples below describe the submission of a single Type II variation under the Centralised Procedure, for 2 marketing authorisations, that is subject to a worksharing agreement.

```
<envelope country="emea">
  <submission type="var-type2" mode="worksharing">
    <number>EMEA/H/XXXX/WS/005</number>
    <tracking>
      <number>EMEA/H/C/000123/WS005/023</number>
    </tracking>
  </submission>
  …
</envelope>
```

```
<envelope country="emea">
  <submission type="var-type2" mode="worksharing">
    <number>EMEA/H/XXXX/WS/005</number>
    <tracking>
      <number>EMEA/H/C/000456/WS005/037</number>
    </tracking>
  </submission>
  …
</envelope>
```

Note that the high-level worksharing number is assigned by the EMEA/regulatory agency/regulatory tracking system, and therefore might not be known by the applicant/MAH for the first submission. In such cases the relevant part of the value should be populated as "xxxx" for this element for the first submission of the procedure. Once defined by the Agency, the high-level worksharing number should be used in the subsequent submissions.

## Annex 4: Usage of Related Sequences

When submitting an eCTD submission in "grouping" or "worksharing" mode that impacts several marketing authorisations, attention must be paid to the definition of 'sequence' and 'related sequence' fields.

Please note that in eCTD, the lifecycle management is per product, and therefore, for each separate product application, a separate eCTD sequence should be created. (The ICH eCTD v3.x specification only allows the submissions of information relating to a single marketing authorisation. Therefore, when submitting a grouping or worksharing of variations, the eCTD submissions must be copied per marketing authorisation.)

The envelope for each product must specify only the impacted marketing authorisations in question, as described Annex 3. The 'sequence' and 'related sequence' fields will also need to be specified for each impacted eCTD Application, as these are specific to each individual eCTD Application (marketing authorisation) lifecycle. Similarly, the lifecycle management needs to be precise in identifying which application and sequence it applies to. Even though the changes are the same across marketing authorisations, the files impacted, and possibly the files targeted for modification, may not be the same in every impacted marketing authorisation.

The example below illustrates a possible scenario where a worksharing submission of a type II variation covers 2 products. The submission in question is the submission of responses to questions for the variation, at a mid-point in the procedure.

Product A:
- The next available sequence number for this product is 0036
- Variation procedure number, if single, would be EMEA/H/C/000123/II/024
- The eCTD sequence that started the variation activity was 0033
- The impacted file is identified with id "a-123"

Product B:
- The next available sequence number for this product is 0057
- Variation procedure number, if single, would be EMEA/H/C/000456/II/045
- The eCTD sequence that started the variation activity was 0056
- The impacted file is identified with id "b-456"

For both Products A and B, the envelope will contain the same "submission" field (high-level worksharing number), with identification in each separate envelope for each product of the relevant tracking number (variation procedure number) (cf. Annex 3).

For Product A, the sequence is "0036" and the related sequence "0033". The replaced file must be provided in the context of Product A, by referring to the file that was submitted e.g. as part of the sequence "0033". The submission file might then contain:

```xml
<envelope country="emea">
  <submission type="var-type2" mode="worksharing">
    <number>EMEA/H/XXXX/WS/008</number>
    <tracking>
      <number>EMEA/H/C/000123/WS008/024</number>
    </tracking>
  </submission>
  …
  <sequence>0036</sequence>
  <related-sequence>0033</related-sequence>
  …
</envelope>
<m1-eu>
  …
    <leaf ID="a-123" operation="replace" checksum="…" checksum-type="md5"
      xlink:href="<file-path>"
      modified-file="../../../0033/m1/eu/eu-regional.xml#a-123">
```

```
            <title>…</title>
         </leaf>
      …
   </m1-eu>
 </eu:eu-backbone>
```

Similarly, for Product B the sequence is "0057" and the related sequence "0056". The replaced file must be provided in the context of Product B, by referring to the file that was submitted e.g. as part of the sequence "0056". The submission file might then contain:

```
   <envelope country="emea">
      <submission type="var-type2" mode="worksharing">
         <number>EMEA/H/XXXX/WS/008</number>
         <tracking>
            <number>EMEA/H/C/000456/WS008/045</number>
         </tracking>
      </submission>
      …
      <sequence>0057</sequence>
      <related-sequence>0056</related-sequence>
      …
   </envelope>
   <m1-eu>
      …
         <leaf ID="b-456" operation="replace" checksum="…" checksum-type="md5"
           xlink:href="<file-path>"
           modified-file="../../../0056/m1/eu/eu-regional.xml#b-456">
           <title>…</title>
         </leaf>
      …
   </m1-eu>
 </eu:eu-backbone>
```