Active Substance Master File (ASMF) worksharing procedure

The EU/ASMF repository number

Initial ASMF submissions

Dr Nienke Rodenhuis
Joint Working Group on ASMF Procedure & Regulatory Project Leader, Medicines Evaluation Board (CBG-MEB), NL August 2018
The EU/ASMF Repository Number

- The EU/ASMF Repository Number is a centralised, version specific ASMF identification number, assigned by the ASMF Assessment Report Repository, that will allow Competent Authorities to track where the same version of the ASMF is used within Europe

EU/ASMF/XXXXX/YYYY

- where
  - EU/ASMF/XXXXX is the EU/ASMF Reference Number, which is sequentially assigned to the ASMF in order of request, independently of the ASMF holder and active substance
  - YYYY is the Assessment Report Number, which is sequentially assigned to the version of the ASMF. It applies to the entire version of the ASMF submitted in the MAA / MAV application, regardless of whether the AP and/or RP have been updated – also includes subsequent ASMF updates, provided in response to deficiency questions
  - Each version of the ASMF that has been accepted for use in a medicinal product will have a corresponding assessment report
What do I do with the EU/ASMF Repository Number?

The EU/ASMF Repository Number should be used in ALL correspondence relating to the version of the worksharing ASMF, including the ID in eCTD/NeeS sequences.

Note: Competent Authorities may issue additional national ASMF reference numbers for their own national administrative reasons.
How do I get an EU/ASMF Reference Number?

• To obtain a EU/ASMF/XXXXX Reference Number, the ASMF holder should submit a completed **EU/ASMF Reference Number request form** to the RMS/EMA of the associated DCP/CAP procedure.

• List of Contact Points for requesting an EU/ASMF/XXXXX Reference Number will be published on the webpage for the CMD Joint Working Group on ASMF procedures.
National contact points providing the EU/ASMF Reference Number

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>E-MAIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUROPEAN MEDICINES AGENCY</td>
<td><a href="mailto:PA-BUS@ema.europa.eu">PA-BUS@ema.europa.eu</a></td>
</tr>
<tr>
<td>AUSTRIA</td>
<td><a href="mailto:rms@ages.at">rms@ages.at</a></td>
</tr>
<tr>
<td>BELGIUM</td>
<td><a href="mailto:asmfnumber@flagg-afmps.be">asmfnumber@flagg-afmps.be</a></td>
</tr>
<tr>
<td>BULGARIA</td>
<td><a href="mailto:ASMF@bda.bg">ASMF@bda.bg</a></td>
</tr>
<tr>
<td>CROATIA</td>
<td><a href="mailto:ASMF@halmed.hr">ASMF@halmed.hr</a></td>
</tr>
<tr>
<td>CYPRUS</td>
<td><a href="mailto:gtheophanous@phs.moh.gov.cy">gtheophanous@phs.moh.gov.cy</a></td>
</tr>
<tr>
<td>CZECH REPUBLIC - human</td>
<td><a href="mailto:ASMF@suik.cz">ASMF@suik.cz</a></td>
</tr>
<tr>
<td>CZECH REPUBLIC - veterinary</td>
<td><a href="mailto:suchy@uskvbl.cz">suchy@uskvbl.cz</a></td>
</tr>
<tr>
<td>DENMARK</td>
<td><a href="mailto:licensing@dkma.dk">licensing@dkma.dk</a></td>
</tr>
<tr>
<td>ESTONIA</td>
<td><a href="mailto:mrp@avimiamet.ee">mrp@avimiamet.ee</a></td>
</tr>
<tr>
<td>FINLAND</td>
<td><a href="mailto:mrp@timea.lt">mrp@timea.lt</a></td>
</tr>
<tr>
<td>FRANCE - human</td>
<td><a href="mailto:DMF-ASMF@ansm.sante.fr">DMF-ASMF@ansm.sante.fr</a></td>
</tr>
<tr>
<td></td>
<td><a href="mailto:Beatrice.blaisot@ansm.sante.fr">Beatrice.blaisot@ansm.sante.fr</a></td>
</tr>
<tr>
<td></td>
<td><a href="mailto:Maryam.mehmandoust@ansm.sante.fr">Maryam.mehmandoust@ansm.sante.fr</a></td>
</tr>
<tr>
<td>FRANCE - veterinary</td>
<td><a href="mailto:enreg@anses.fr">enreg@anses.fr</a></td>
</tr>
<tr>
<td>GERMANY (BfArM) - human</td>
<td><a href="mailto:Petra.Wagner@bfarm.de">Petra.Wagner@bfarm.de</a></td>
</tr>
<tr>
<td>Germany (BVL) - veterinary</td>
<td><a href="mailto:asmf@bvl.bund.de">asmf@bvl.bund.de</a></td>
</tr>
<tr>
<td>GREECE</td>
<td><a href="mailto:vviolakis@eof.gr">vviolakis@eof.gr</a></td>
</tr>
<tr>
<td></td>
<td><a href="mailto:ppagriotoula@eof.gr">ppagriotoula@eof.gr</a></td>
</tr>
<tr>
<td>HUNGARY</td>
<td><a href="mailto:mrp-dcp-new-rms@ogyei.gov.hu">mrp-dcp-new-rms@ogyei.gov.hu</a></td>
</tr>
<tr>
<td>ICELAND</td>
<td><a href="mailto:Ulrike.Muus@lyfjastofnun.is">Ulrike.Muus@lyfjastofnun.is</a></td>
</tr>
<tr>
<td>IRELAND</td>
<td><a href="mailto:submissions@hpria.ie">submissions@hpria.ie</a></td>
</tr>
<tr>
<td>ITALY</td>
<td><a href="mailto:f.cavalleraro@aifa.gov.it">f.cavalleraro@aifa.gov.it</a></td>
</tr>
<tr>
<td>LATVIA</td>
<td><a href="mailto:ASMF@zva.gov.lv">ASMF@zva.gov.lv</a></td>
</tr>
<tr>
<td>LIECHTENSTEIN</td>
<td><a href="mailto:rms@ages.at">rms@ages.at</a></td>
</tr>
<tr>
<td>LITHUANIA</td>
<td><a href="mailto:ilonaalisauksiene@vvkt.lt">ilonaalisauksiene@vvkt.lt</a></td>
</tr>
<tr>
<td>LUXEMBOURG</td>
<td><a href="mailto:Jacqueline.genoux-hames@ms.etat.lu">Jacqueline.genoux-hames@ms.etat.lu</a></td>
</tr>
<tr>
<td>MALTA</td>
<td><a href="mailto:mrp-dcp.adm@gov.mt">mrp-dcp.adm@gov.mt</a></td>
</tr>
<tr>
<td>THE NETHERLANDS</td>
<td><a href="mailto:Dienstpostbuszcmdh@cbo-meb.nl">Dienstpostbuszcmdh@cbo-meb.nl</a></td>
</tr>
<tr>
<td>NORWAY</td>
<td><a href="mailto:pk@legemiddelverket.no">pk@legemiddelverket.no</a></td>
</tr>
<tr>
<td>POLAND</td>
<td><a href="mailto:Joanna.bokus@urpfl.gov.pl">Joanna.bokus@urpfl.gov.pl</a></td>
</tr>
<tr>
<td>PORTUGAL</td>
<td><a href="mailto:dam@infarmed.pt">dam@infarmed.pt</a></td>
</tr>
<tr>
<td>ROMANIA</td>
<td><a href="mailto:mrp-dcp.info@anm.ro">mrp-dcp.info@anm.ro</a></td>
</tr>
<tr>
<td>SLOVAK REPUBLIC</td>
<td><a href="mailto:maria.pollakova@suik.sk">maria.pollakova@suik.sk</a></td>
</tr>
<tr>
<td>SLOVENIA</td>
<td><a href="mailto:asmf_aemp@aemp.es">asmf_aemp@aemp.es</a></td>
</tr>
<tr>
<td>SPAIN</td>
<td><a href="mailto:RIC@mpa.se">RIC@mpa.se</a></td>
</tr>
<tr>
<td>UNITED KINGDOM - human</td>
<td><a href="mailto:Mr-dcpprocedures@mhra.gsi.gov.uk">Mr-dcpprocedures@mhra.gsi.gov.uk</a></td>
</tr>
<tr>
<td>UNITED KINGDOM - veterinary</td>
<td><a href="mailto:i.jenkins@vmd.defra.gsi.gov.uk">i.jenkins@vmd.defra.gsi.gov.uk</a></td>
</tr>
</tbody>
</table>
EU/ASMF Reference Number request form - Template

EU ASMF number request form

(from ACTIVE SUBSTANCE MASTER FILE HOLDER ON HEADED PAPER)

From: <ASMF Holder name>
<ASMF Holder address>
<ASMF Holder Post code/Town>
<ASMF Holder Country>

To: <Name and Address of Competent Authority>

(subjects) Submission of request for EU/ASMF/XXXXXXXX number

Date: <Date>

Dear Sir or Madam,

This Active Substance Master File will be submitted in relation to the following procedure:

<table>
<thead>
<tr>
<th>Medicinal product</th>
<th>Name of the medicinal product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocated procedure number</td>
<td>EMEA/Art. product reference number/procedure reference</td>
</tr>
<tr>
<td>(unaudited) Submission date of the marketing authorisation application (if different)</td>
<td>DD/MM/YYYY</td>
</tr>
</tbody>
</table>

Yours faithfully,

Signature of authorised contact person

Name, address and position in company

Mandatory administrative details for obtaining an EU ASMF number

This request form should be used for an Active Substance Master File to be assessed as part of a new marketing authorisation through the Centralised or Decentralised procedure only, where a full assessment report will be prepared by a Competent Authority.

In line with the current scope of the ASMF work-sharing procedure, a new ASMF is defined as an ASMF that has not been previously assessed by a Competent Authority as part of a Centralised, Decentralised or Mutual Recognition new marketing authorisation or variation application. It is expected that a new ASMF may have been assessed as part of a national application.

Where the ASMF holder already holds an ASMF that has been assigned an EU/ASMF reference number and wishes to register another ASMF for the same active substance, e.g. a substantially different route of synthesis (see Annex 1 Assignment of a new ASMF Reference Number), this should also be clearly stated in the Additional Information field.

<table>
<thead>
<tr>
<th>ASMF holder and address</th>
<th>&lt;ASMF Holder name&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active substance name</td>
<td>EIN, common name (+ 200/weight when applicable)</td>
</tr>
<tr>
<td>Active Substance Manufacturer</td>
<td>Internal drug substance/API code (if applicable)</td>
</tr>
<tr>
<td>ASMF holder’s version (as included in the future submission)</td>
<td>Applicants part; version [version number]/date (dd-mm-yyyy)</td>
</tr>
<tr>
<td>Restricted part; version [version number]/date (dd-mm-yyyy)</td>
<td></td>
</tr>
</tbody>
</table>

Additional information (if applicable, e.g. different route of synthesis, particle size distribution)

1 EU/ASMF/XXXXXXX reference number is allocated from the CTS ASMF assessment report repository by the Competent Authority/EMA.

2 May warrant issue of a new EU/ASMF number.
EU/ASMF Reference Number request form - Example

ASMF-Holdings Ltd
100 High Street, London, UK
www.ASMF-holdings-ltd.com

EU ASMF number request form

From: ASMF-Holdings Ltd
100 High Street
London, UK

To: Medicines and Healthcare products Regulatory Agency
111 Buckingham Palace Road
Victoria
London
SW1W 9SZ

Date: 1 Oct 2013

Subject: Submission of request for EU/ASMF/XXXX1 number

Dear Sir or Madame,

This Active Substance Master File will be submitted in relation to the following procedure:

Medicinal product
Allocated procedure number
(Intended) Submission date of the marketing authorisation application (if known)

Accord 2.5mg, 5mg, 7.5mg, 10mg, 15mg and 20mg film-coated tablets
UK/W/699999/01-06/DC
12/November/2013

Mandatory administrative details for obtaining an EU ASMF number

This request form should be used for an Active Substance Master File to be assessed as part of a new marketing authorisation through the Centralised or Decentralised procedure only, where a full assessment report will be prepared by a Competent Authority.

In line with the current scope of the ASMF work sharing procedure, a new ASMF is defined as an ASMF that has not been previously assessed by a Competent Authority as part of a Centralised, Decentralised or Mutual Recognition new marketing authorisation or variation application - it is accepted that a new ASMF may have been assessed as part of a national application.

Where the ASMF holder already holds an ASMF that has been assigned an EU/ASMF reference number and wishes to register another ASMF for the same active substance, e.g. a substantially different route of synthesis (see Annex 1 Assignment of a new ASMF Reference Number), this should also be clearly stated in the Additional Information field.

<table>
<thead>
<tr>
<th>ASMF Holder and address</th>
<th>ASMF Holdings Ltd 100 High Street London, UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active substance name</td>
<td>Accord</td>
</tr>
</tbody>
</table>
| Active Substance
  Manufacturer’s
  internal drug
  substance/API code (if applicable) | ACE                                         |
| ASMF Holder’s version (as included in the future submission) | Applicants part  Version [version number]/data (dd-mm-yyyy)  Restricted part  Version [version number]/date (dd-mm-yyyy) |

Additional Information (as applicable, e.g. different routes of synthesis, particle size distribution)2

Yours faithfully,

Dr RA Smith
Head of Regulatory Affairs
ASMF-Holdings Ltd

1 EU/ASMF/XXXX reference number is allocated from the CTS ASMF assessment report repository by the Competent Authority/EMA

2 May warrant issue of a new EU/ASMF number.
EU/ASMF Reference Number request form - Example

ASMF-Holdings Ltd
100 High Street, London, UK
www.ASMF-holdings-ltd.com

EU ASMF number request form

From: ASMF-Holdings Ltd
100 High Street
London, UK

To: Medicines and Healthcare products Regulatory Agency
151 Buckingham Palace Road.
Victoria,
London,
SW1W 9SZ

Subject: Submission of request for EU/ASMF/XXXXX number

1 Oct 2013

Name & address of Competent Authority

ASMF holder’s headed paper

ASMF holder’s address

Date
EU/ASMF Reference Number request form - Example

Subject: Submission of request for EU/ASMF/XXXXX number

Dear Sir or Madam:

This Active Substance Master File will be submitted in relation to the following procedure:

<table>
<thead>
<tr>
<th>Medicinal product</th>
<th>Allocated procedure number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aceopril 2.5mg, 5mg, 7.5mg, 10mg, 15mg and 20mg film-coated tablets</td>
<td>UK/H/99999/01-06/DC</td>
</tr>
</tbody>
</table>

(Intended) Submission date of the marketing authorisation application (if known)
12/October 2013

Yours faithfully,
Dr RA Smith
Head of Regulatory Affairs
ASMF-holdings Ltd

Name of the medicinal product
DCP/CAP procedure number
Intended submission date for the medicinal product, if known
Name, address of position of the authorised contact person for the ASMF holder
Signature of the authorised contact person
EU/ASMF Reference Number request form - Example

Mandatory administrative details for obtaining an EU ASMF number

This request form should be used for an Active Substance Master File to be assessed as part of a new marketing authorisation through the Centralised or Decentralised procedure only, where a full assessment report will be prepared by a Competent Authority.

In line with the current scope of the ASMF work sharing procedure, a 'new ASMF' is defined as an ASMF that has not been previously assessed by a Competent Authority as part of a Centralised, Decentralised or Mutual Recognition new marketing authorisation or variation application - it is accepted that a 'new ASMF' may have been assessed as part of a national application.

Where the ASMF holder already holds an ASMF that has been assigned an EU/ASMF reference number and wishes to register another ASMF for the same active substance, e.g. a substantially different route of synthesis (see Annex 1 Assignment of a new ASMF Reference Number), this should also be clearly stated in the Additional information field.

<table>
<thead>
<tr>
<th>ASMF Holder and address</th>
<th>&lt;ASMF Holder name&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active substance name</td>
<td>&lt;INN, common name&gt; (+ salt/water content when applicable)</td>
</tr>
<tr>
<td>Active Substance Manufacturer’s internal drug substance/API code (if applicable)</td>
<td></td>
</tr>
<tr>
<td>ASMF Holder’s version (as included in the future submission)</td>
<td>Applicants part: Version [version number]/date (dd-mm-yyyy) Restricted part: Version [version number]/date (dd-mm-yyyy)</td>
</tr>
<tr>
<td>Has this ASMF already been assessed?</td>
<td>Yes / No ²</td>
</tr>
<tr>
<td>Additional information (as applicable, e.g. different route of synthesis, particle size distribution) ³</td>
<td></td>
</tr>
</tbody>
</table>

ASMF holder’s name & address
Active substance name & Active Substance Manufacturer’s API code
Version numbers of Applicant’s and Restricted Parts of the ASMF
Include whether ASMF has been assessed before
Submitting the EU/ASMF Reference Number request form

• The EU/ASMF Reference Number request form should be submitted **no more than 2 weeks** before the intended ASMF submission date.

• The Competent Authorities will issue the EU/ASMF/XXXXX reference number **within 10 days** of the request.

• An EU/ASMF reference number **will not be issued without an associated DCP/CAP number** to prevent ASMF holders reserving reference numbers ‘**en bloc**’
  – ASMF holders should discuss intended MA submission dates with the MA applicants and use the procedure with the earliest submission date in the request form.
The Assessment Report Number & the EU/ASMF Repository Number

• At ASMF submission, the ASMF-AR repository will assign the 0001 Assessment Report Number to the initial version of the ASMF e.g.

  EU/ASMF/99999/0001
  Applicant’s Part: ACE/AP/01/2010-03-28
  Restricted Part: ACE/RP/01/2010-03-28

• Therefore, the EU/ASMF Repository Number identifies the version of the ASMF

• Once the EU/ASMF repository number has been assigned to the version of the ASMF, it can then be communicated to all Applicants
  – A change to the submission date of the procedure used to obtain the EU/ASMF reference number will not impact other procedures
Creating an EU/ASMF repository record for the ASMF

• The Competent Authority will use the information in the EU/ASMF reference request form to create a record for the ASMF in the ASMF assessment report repository

• The information provided in the EU/ASMF reference request form is sufficient to identify duplicate records for the same ASMF, therefore, it is important that all fields are completed by the ASMF holder
When can I use the same EU/ASMF reference number?

• The following list of non-exhaustive examples will require a new EU/ASMF/XXXXX reference number*:
  – Different active substance
  – Different set of specification (except when finished product specific):
    • Different salt of an active substance
    • Different complex of an active substance
    • Different solvate or hydrate form of an active substance
    • Different isomer or mixture of isomers of an active substance
    • Opposite enantiomer of an active substance
    • Racemate of an optically pure active substance
  – Introduction of a new substantially different route of synthesis
  – The active substance is used for both human and veterinary medicinal products and is controlled to different quality standards

* As jointly agreed by QWP and CMD
When can I use the same EU/ASMF reference number?

• The same EU/ASMF/XXXXX reference number can be used in the following non-exhaustive examples*:
  – Slightly different routes of synthesis which do not result in changes to important quality characteristics of the active substance, such as the qualitative and/or quantitative impurity profile requiring qualification or physico-chemical properties impacting on bioavailability
  – Different manufacturing sites using the same or similar routes of synthesis
  – Other changes which do not result in a changes to important quality characteristics of the active substance, such as qualitative and/or quantitative impurity profile requiring qualification or physico-chemical properties impacting on bioavailability
  – Transfer of ownership of an existing ASMF from one ASMF holder to another
  – Change in the name and/or address of the existing ASMF holder

• If in doubt, the ASMF holder should consult the appropriate Competent Authority

* As jointly agreed by QWP and CMD
End of Presentation