



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

eAF is mandatory for all procedures – what to consider by applicants

Webinar for the usage of an eAF by applicants

Presented by: Georg Neuwirther, Klaus Menges and Kristiina Puusaari
11 January 2016





Agenda

1. Overview and Status

Speaker: Georg Neuwirther (AGES, chair eAF MG)

2. Usage of an eAF at applicants level including Q&As

Speaker: Kristiina Puusaari (EMA) and Klaus Menges (BfArM)

3. Questions and Discussion



OVERVIEW AND STATUS



eAF Maintenance Group (eAF MG)

- Group of business and IT-experts from NCAs, EMA and Industry
- eAF MG is in charge of implementing the eAF according to the eSubmission Roadmap
- Evolution: 1. word AF -> 2. eAF -> 3. Single Submission Portal

- Please contact us via eaf@ema.europa.eu for any questions!

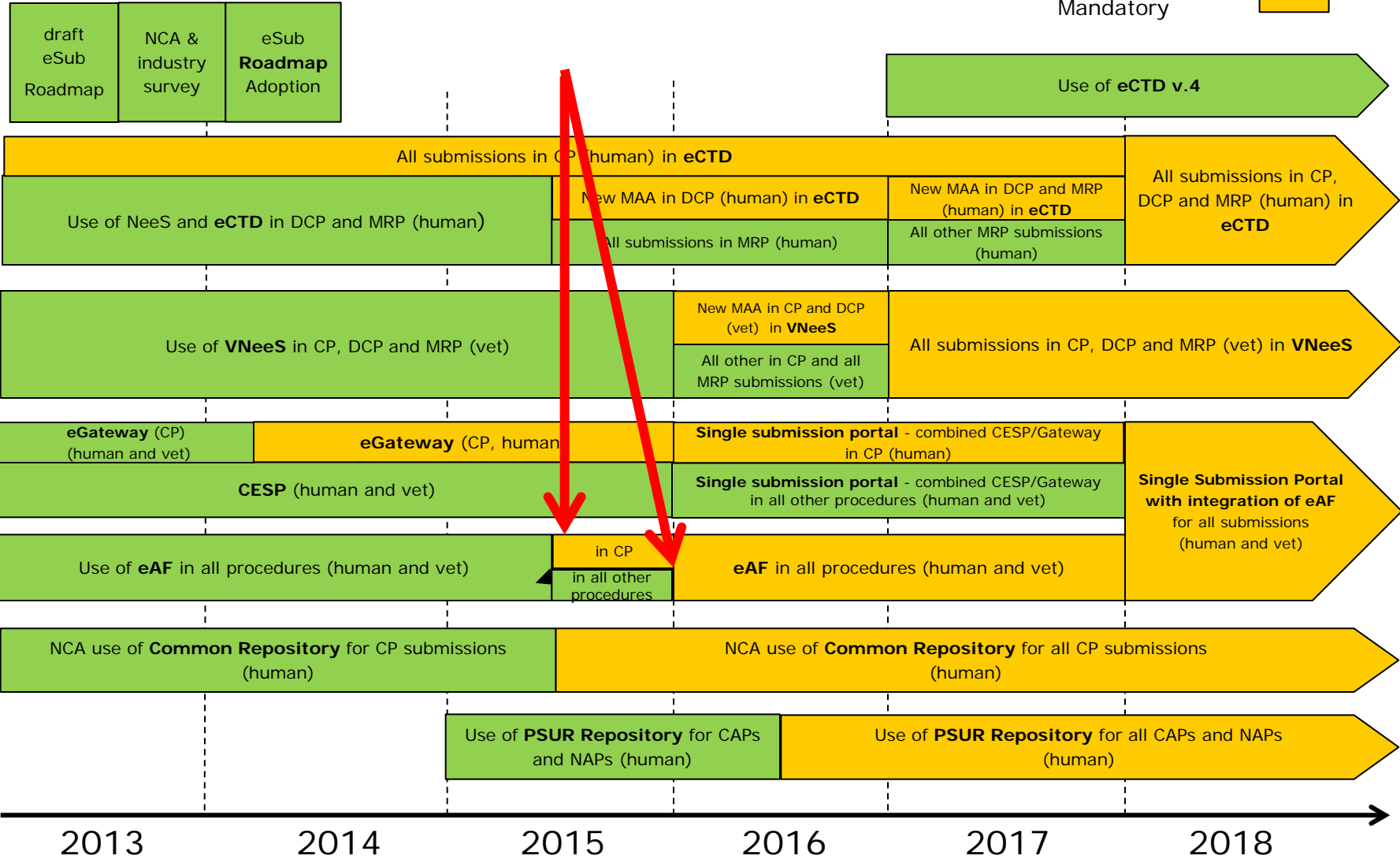
Background eSubmission Roadmap



EUROPEAN MEDICINES AGENCY

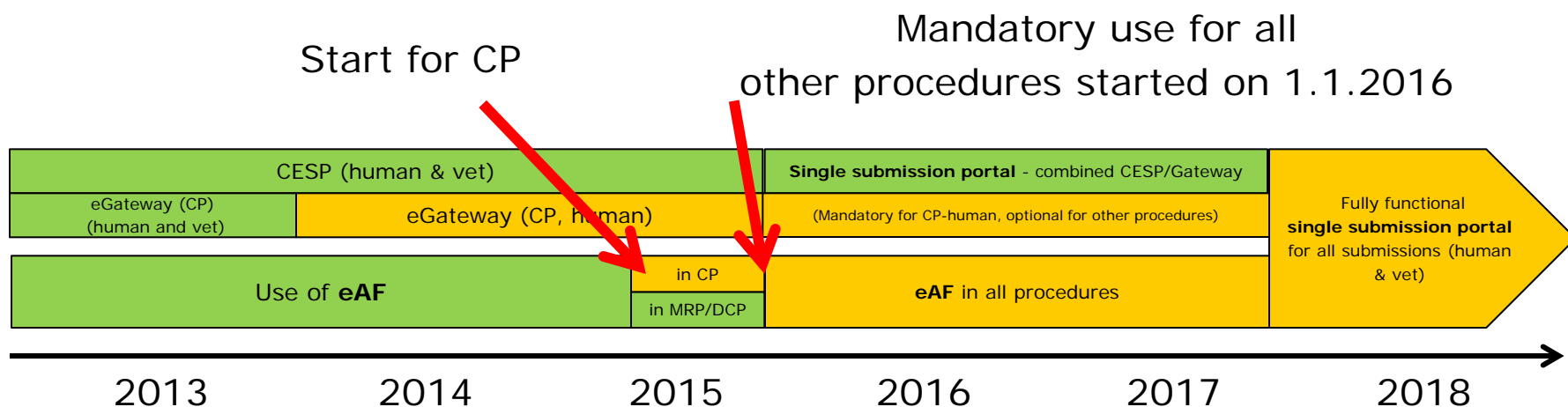
(reflecting final adopted version 1.0 dated 07/11/14)

Ongoing/optional █
Mandatory █



Successful start of compulsory usage of the eAF for Centralised Procedures (all types; Marketing Authorisation Applications, variations and renewals for human & veterinary) on the 1st of July 2015

- Current figures: only <1% of CP submissions do not contain eAF-compliant application forms! Non-compliant submissions are rejected and resubmission is requested.
- Please ensure to use the correct eAF-version
- Please do not print and scan the eAF! This will delay the application!





Option 1 - link to eAF webpage from Eudralex page

Notice to Applicants (European Commission)

- <http://ec.europa.eu/health/documents/eudralex/vol-2>
- http://ec.europa.eu/health/documents/eudralex/vol-6/index_en.htm

Note: The Word-AFs have been removed from the Eudralex website!

Option 2

eSubmission Homepage (EMA)

<http://esubmission.ema.europa.eu/eaf/index.html>

Release Plan

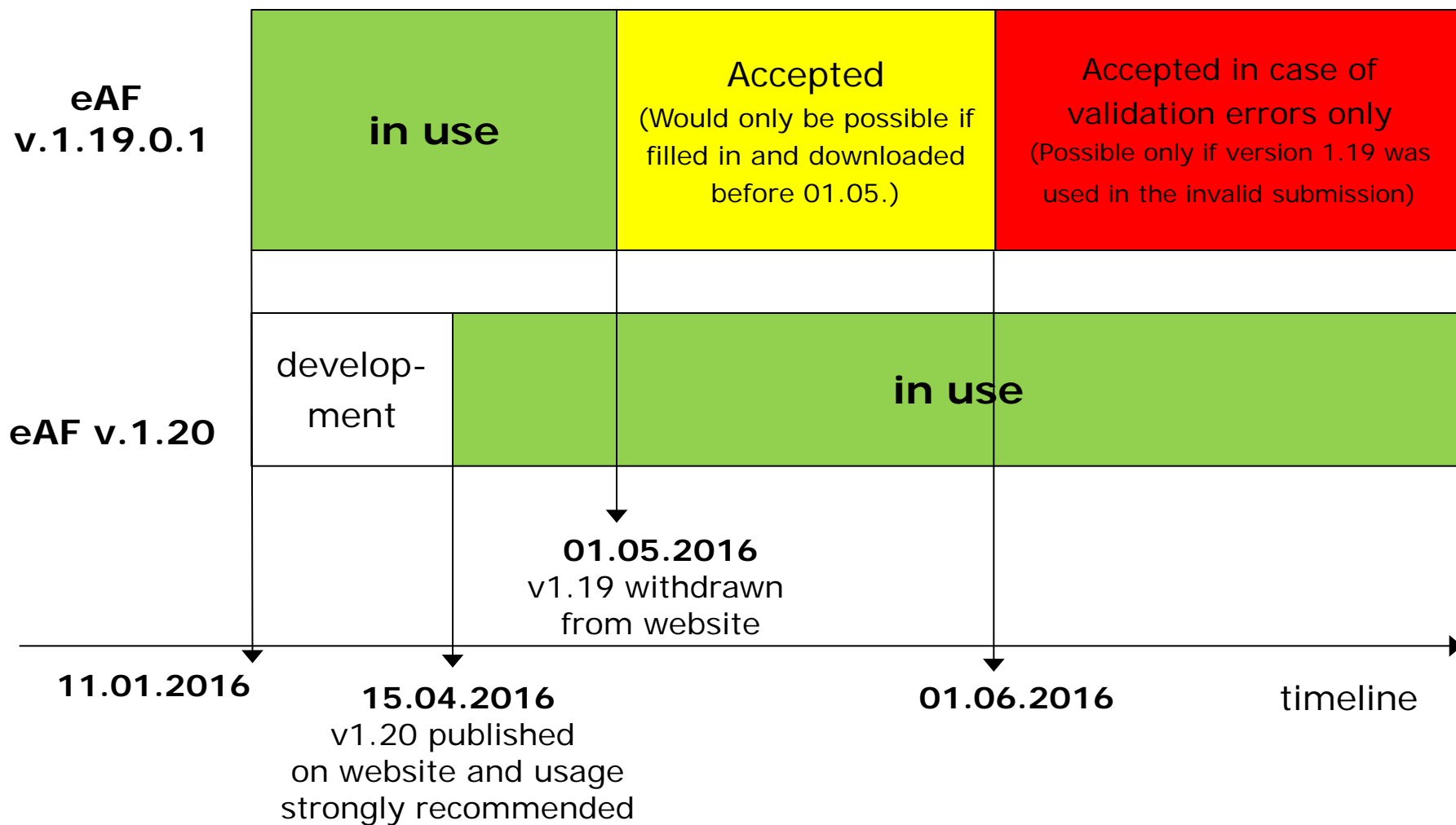
published here: <http://esubmission.ema.europa.eu/eaf/index.html>

Excerpt of Release Plan (status 30.11.2015)

Please check website for updates!

Milestone	Date
Publication of eAF version 1.19.0.1	30/11/15
eAF v01.19.0.1 replaces all previous versions (v1.19, v1.18,...)	11/01/16 Older versions will not be accepted after this date for new submissions
Publication of eAF version 1.20	15/04/16

Current detail plan for eAF v.1.20





Why guidance documents – eAF contains the same data as before?

yes, and ...

- eAFs provide less free text sections, defines more data structure and makes use of controlled terms (EUTCT)
- Provides features which were not possible with WORD

Change process for applicants and agencies!

— Guidance Documents

Regulatory

[User Guide for the electronic application form for a marketing authorisation \(Human\)](#) **New**

[User Guide for the electronic application form for a marketing authorisation \(Veterinary\)](#) **New**

Technical

[Technical guidance Human and Vet \(19/10/2015\)](#) **New**

Q & A

[User Guidance Human & Vet](#)

[Questions and Answers \(19/10/2015\)](#) **New**

[Benchmark response times](#)

[eAF performance](#)



- Check IT infrastructure (Adobe reader version 10 or above)
- Check internet-connectivity to EUTCT (e.g. for search for substances)
- Update internal guidelines and offer internal trainings
- Organise templates for AFs
 - Usage of XML-files, "Save-AS"
- Be prepared for updates of eAFs
 - Check eAF website for Release Plan and Release Notes
 - User Acceptance Tests will be announced
- Evaluate automated data import into eAF (from industry IT systems)
 - A data exchange standard is published on the eAF-website



- Scope of the eAFs
- eAF support structure
- Impact of mandatory use
- Receipt and validation
- Look and feel
- Navigation
- Locking the form and signatures
- Form validation
- Controlled terminology and Term Request Process for EUTCT
- Workarounds
- Known defects
- How to submit in VNeS, NeS and eCTD, examples in human areas how do it best (file naming)
- XML Export and Import
- Q&A



- The eAFs have now replaced the Notice to Applicants (NTA) Initial Human and Veterinary **MAA** forms, **Variation** form and the **Renewal** application forms
- The eAFs must be used for all Human and Veterinary submissions for Centralised Procedure and MRP/DCP and National Procedures
- The **Homeopathic** form and all other EMA or NCA specific forms, for example the **pre-submission form** or the **61(3) notification form** remain in their existing formats – they are currently **out of the scope** of the eAF project



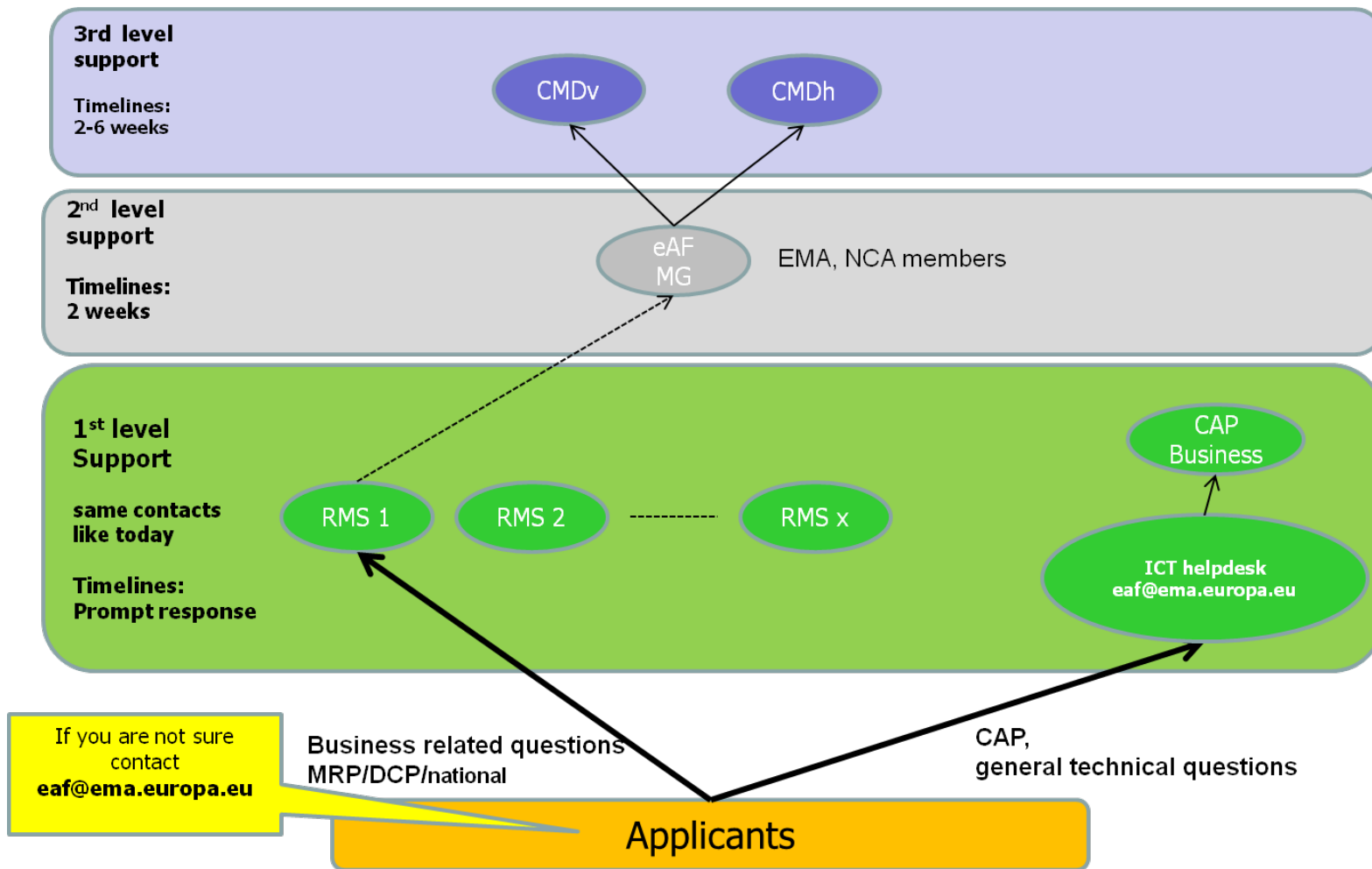
Why will support be needed?

- Technical change from Word to PDF format
- eAF structure cannot be changed by the applicant like Word forms
- Majority of free text fields have been replaced by controlled vocabularies – terms are selected from EUTCT-catalogues – if terms are not available they should be requested through [MDMS new term request process](#). All requests should be sent to the mdms@ema.europa.eu email address.
- Paper forms were isolated documents with no direct IT-integration into the business process (e.g. for automatic data import). Now eAF data will be used directly in IT-systems reducing manual workload and human error



- Technical questions, comments, change requests – send your questions to eAF@ema.europa.eu
- New term requests: mdms@ema.europa.eu

- Procedural questions
 - CP – eAF@ema.europa.eu
 - MRP/DCP/NP– if questions are received to eAF@ema.europa.eu and are very specific to a particular NCA/application the applicant is advised to contact the RMS/relevant NCA using the normal channels for queries to the NCAs.
 - Mixed queries containing both technical and procedural queries should be sent directly to RMS/NCA – RMS/NCA may forward the reply to eAF@ema.europa.eu and EMA will complete response with the technical details and will reply directly to the applicant with NCA in copy.
 - Mixed queries containing both technical and procedural queries received by EMA – EMA will reply to the user providing response on the technical issue and will direct the applicant to RMS/NCA for the procedure aspects





- The mandatory use for all procedure types has started on 1st January 2016 as planned – the forms are available from the [eAF website](#)
- The eAFs should be submitted as ‘real’ eAFs – meaning that they are kept in electronic format and are submitted with the xml. Forms that have been printed and scanned as PDF lose all their intelligent features and become flat PDFs. These do not allow import/export of xml data into receiving systems. Scanned eAFs may be rejected by receiving regulators!
- The eAFs are mandatory also for submissions where the product lifecycle is paper based – i.e. eAFs must be used also for paper submissions (NTA form is replaced by eAF which can be printed and included within the paper dossier if required)
- The mandatory use of the eAFs **does not change** any existing **wet signature requirements** by the NCAs – only the form changes – i.e. instead of the word or pdf version of the AF available in the NTA Eudralex website the only forms available now are the PDF eAFs.
- The form should be inserted in the same location in the submission package as before.



- Completing the form is based on controlled terminologies and is less flexible than using the paper forms. You should check at an early stage whether all terms needed are available via the form. If terms are not available through the form you should request new terms using the defined new term request process (send request form to mdms@ema.europa.eu).
- Applicants should note that it will take slightly longer to open to the eAF PDFs than the paper application forms. This is due to the build in business rules and the controlled terminologies in the forms. Approximate opening times have been gathered and are published on the eAF website on a document called [eAF performance](#). EMA is continuously working hard to improve the performance of the forms.



Form versions

- The Notice to Applicants (NTA) application forms are updated regularly and to ensure that the eAF corresponds with the latest NTA forms new versions of the eAFs are launched. Majority of the eAF versions include changes implemented in NTA forms. Alongside these changes, additional usability improvements are provided based on prioritised change requests. NTA announces a date for mandatory use of the new versions.
For releases without any NTA changes, the mandatory use date is decided together with the network at the eAF maintenance group (MG)
- Version 1.19 of the eAFs is reflecting changes in the NTA initial MAA form and additionally, number of change requests have been implemented in all four forms. All implemented change requests are listed on the eAF [release notes](#) available on the eAF webpage.
- Version 1.20 will bring further bug fixes and usability improvements based on change requests prioritised by the eAF MG (consisting of NCAs and industry).



- All applications submitted after 1 January 2016 should be submitted in eAF format – it is the applicants responsibility to provide the application using the correct version of the eAFs
- After 1 January 2016 the NTA paper forms are only accepted **for ongoing procedures** – You should **not** convert from NTA paper form to an eAF in the **middle** of the procedure!
- As usual, previous versions of the forms are accepted for ongoing procedures – there is no need to update the form version in the middle of the procedure
- As with any application form – the eAFs should be provided as a part of the submission package i.e. for eCTD submissions the eAF should be included **inside the eCTD or NeeS** structure in Module 1 folder 1.2.
- In VNeedS submissions the eAF should be provided as a part of the submission as previously



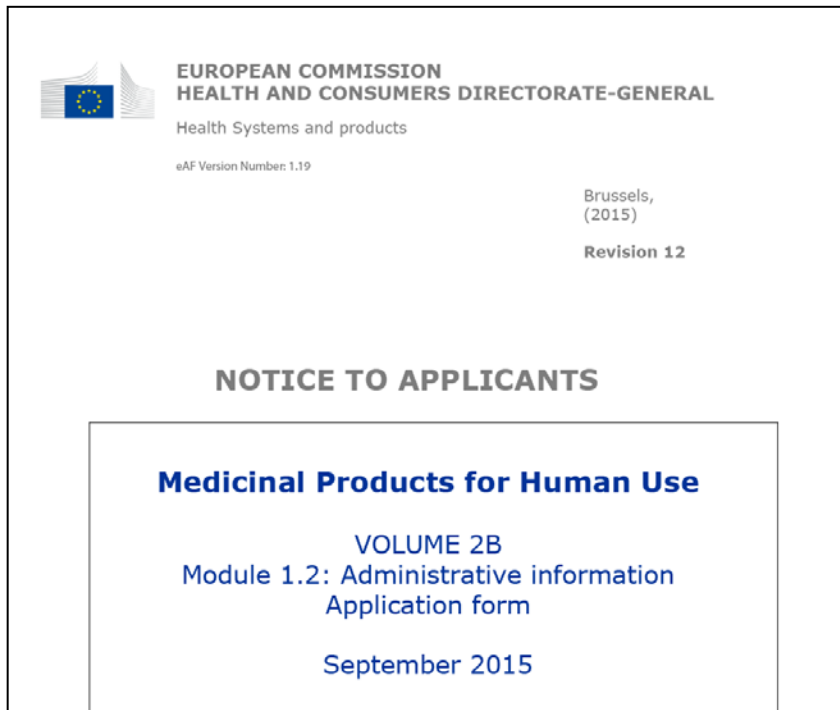
- The eAFs should not be sent as a separate email or CESP submissions.
- The eAF should be provided in PDF format within the submission.
- The applicants should not provide the xml extraction along with the submission data as it would lead to a need to check that the xml and the PDF are identical.
- The receiving NCAs will extract the xml where necessary for their business processes.
- There should be **no bookmarks** within the eAFs! The bookmarks may cause validation issues and lead to delays!
- A known issue with the Fast Web View not being compatible with eAFs – eCTD and NeeS validation tools will give Best Practice error which should be ignored.



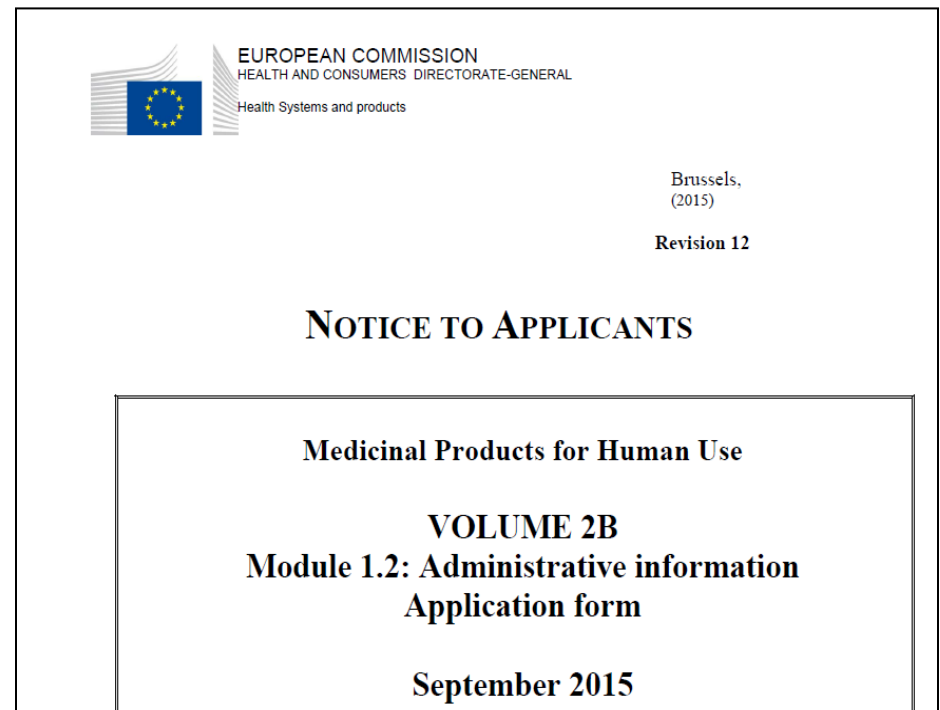
- You can recognise the eAFs easily as they look different from the NTA paper forms, see example below of :

– the Initial H-MAA:

eAF



Paper form





– the Initial V-MAA:

eAF



**EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL**

Consumer goods
Pharmaceuticals

eAF Version Number: 1.19

Brussels, 01.06.2015

Revision 7.4

NOTICE TO APPLICANTS

Medicinal Products for Veterinary Use

VOLUME 6B

**Presentation and content of the dossier-Part 1
Summary of the dossier Part 1A
Application form**

June 2015

Paper form



**EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE GENERAL**

Health Systems and products

Brussels, 01.06.2015

Revision 7.4

NOTICE TO APPLICANTS

Medicinal products for veterinary use

VOLUME 6B

**Presentation and content of the dossier-Part 1
Summary of the dossier Part 1A
Application form**

June 2015

Note: The error in the European Commission header for the initial V-MAA eAF has been noticed and will be updated in the next release of the eAF.



– the Variation application:

eAF

Paper form



EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health Systems and products

eAF Version Number: 1.19

June 2015

NOTICE TO APPLICANTS

APPLICATION FOR VARIATION TO A MARKETING AUTHORISATION

June 2015

APPLICATION FOR VARIATION TO A MARKETING AUTHORISATION

HUMAN

VETERINARY

NATIONAL AUTHORISATION IN MRP Variation procedure number(s)¹:

NATIONAL AUTHORISATION

EU AUTHORISATION: The use of the electronic application forms is mandatory for Centralised Procedure

<http://esubmission.ema.europa.eu/eaf/index.html>

Reference Member State / Reference Authority for worksharing

AT BE BG CY CZ DE DK EE EL ES FI FR HR HU IE
 IS IT LI LT LU LV MT NL NO PL PT RO SE SI SK
 UK

Concerned Member State(s)

AT BE BG CY CZ DE DK EE EL ES FI FR HR HU IE
 IS IT LI LT LU LV MT NL NO PL PT RO SE SI SK
 UK NONE

Type of Application (tick all applicable options)

- | | |
|--|--|
| <input type="checkbox"/> Type IA _{IN} | <input type="checkbox"/> Single variation |
| <input type="checkbox"/> Type IA | <input type="checkbox"/> Grouping of variations |
| <input type="checkbox"/> Type IB unforeseen ² | <input type="checkbox"/> Including a line extension ³ |
| <input type="checkbox"/> Type IB | <input type="checkbox"/> Worksharing |
| <input type="checkbox"/> Type II | |
| <input type="checkbox"/> Type II Art. 29 ⁴ | |



– the renewal application form:

eAF

Paper form



EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

eAF Version Number: 1.19

June 2015

NOTICE TO APPLICANTS

**APPLICATION FORM FOR RENEWAL OF A
MARKETING AUTHORISATION**

June 2015

**APPLICATION FORM FOR RENEWAL OF A MARKETING
AUTHORISATION**

HUMAN VETERINARY

NATIONAL AUTHORISATION IN MRP/DCP MRP/DCP procedure number¹: ____/____/____
NATIONAL AUTHORISATION ONLY

EU AUTHORISATION: The use of the electronic application forms is mandatory for Centralised Procedure
<http://esubmission.ema.europa.eu/eaf/index.html>

Reference Member State:

AT BE BG CY CZ DE DK EE EL ES FI FR HR
HU IE IS IT LI LT LU LV MT NL NO PL PT
RO SE SI SK UK

Concerned Member States:

AT BE BG CY CZ DE DK EE EL ES FI FR HR
HU IE IS IT LI LT LU LV MT NL NO PL PT
RO SE SI SK UK NONE

Is the product currently marketed? Yes No If yes, in which Member States²?

AT BE BG CY CZ DE DK EE EL ES FI FR HR
HU IE IS IT LI LT LU LV MT NL NO PL PT
RO SE SI SK UK

Navigation before and after locking the form

TABLE OF CONTENTS

DECLARATION AND SIGNATURE

1. TYPE OF APPLICATION

- 1.1 This application concerns
- 1.2 Orphan medicinal product information
- 1.3 Application for a change to existing marketing authorisation leading to an extension as referred to in Annex I of Regulations (EC) no 1234/2008, or any national legislation, where applicable
- 1.4 This application submitted in accordance with the following Article 2001/83/EC
- 1.5 Consideration of this application also requested under the following article in Directive 2001/83/EC or Regulation (EC) N° 726/2004
- 1.6 Requirements according to Regulation (EC) No 1901/2006 ('Paediatric Regulation')

2. MARKETING AUTHORISATION APPLICATION PARTICULARS

- 2.1 Name(s) and ATC code
- 2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
- 2.3 Legal status
- 2.4 Marketing authorisation holder / Contact persons / Company
- 2.5 Manufacturers
- 2.6 Qualitative and quantitative composition

3. SCIENTIFIC ADVICE

Click to advance to named section.

4. OTHER MARKETING AUTHORISATION APPLICATIONS

- 4.1 For National/MRP/DCP applications, please complete the following in accordance with Article 8(j)-(l) of Directive 2001/83/EC
- 4.2 Marketing authorisation applications for the same product in the EEA (same qualitative and quantitative composition in active substance(s) and having the same pharmaceutical form from applicants belonging to the same mother company or group of companies OR which are "licensees").
- 4.3 For multiple/duplicate applications of the same medicinal product
- 4.4 Marketing authorisation applications for the same product outside the EEA (i.e from applicants belonging to the same mother company or group of companies OR which are "licensees". Same qualitative and quantitative composition in active substance(s) and having the same pharmaceutical form).

5. ANNEXED DOCUMENTS (where appropriate)

FORM VALIDATION

unlocked

TABLE OF CONTENTS

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Click to advance to named section.

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5. ANNEXED DOCUMENTS (where appropriate)

FORM VALIDATION

locked



unlocked

locked

TABLE OF CONTENTS

1. APPLICATION FOR VARIATION TO A MARKETING AUTHORISATION
 2. PRODUCTS CONCERNED BY THIS APPLICATION⁷
 3. TYPES OF CHANGE(S)
- ANNEXED DOCUMENTS (WHERE APPROPRIATE)
DECLARATION OF THE APPLICANT
SIGNATURE
NOTES
FORM VALIDATION
-

TABLE OF CONTENTS


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FORM VALIDATION
- 

TABLE OF CONTENTS


1. APPLICATION FOR RENEWAL OF A MARKETING AUTHORISATION
 2. APPROVED MANUFACTURERS
 3. QUALITATIVE AND QUANTITATIVE COMPOSITION IN TERMS OF THE ACTIVE SUBSTANCE(S) AND THE EXCIPIENT(S)
- DECLARATION AND SIGNATURE
NOTES
FORM VALIDATION
- 
- Click to advance to named section.
-

TABLE OF CONTENTS

1. APPLICATION FOR RENEWAL OF A MARKETING AUTHORISATION
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- DECLARATION AND SIGNATURE
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FORM VALIDATION
-

Click to advance to named section.



- All eAFs contain built in business validation based on complex validation rules. If you identify incorrect business rules please report to eAF@ema.europa.eu to raise a change request.
- Ideally, all validation errors are solved before finalising, signing and locking the form – it's very important to **save the unlocked forms** before signing them in case there are any validation issues and updated form is requested – **it is not possible to change already locked forms** (signing will lock the form) and in case no unlocked version has been saved you might have to refill the whole form in order to make changes to respond to the validation comments.
- Occasionally it is not possible to solve all validation comments and once the forms are locked the form will display the number of 'form validation errors' at the very end of the form – however it is not possible to see to which sections these validation errors refer to. Validation errors in the form can, in most cases, be ignored as these often refer to sections for which a separate annex has been provided.

FORM VALIDATION

Validation Errors: 0



- The form validation is not a technical eCTD or NeeS/VNeeS validation.
- Leaving validation errors in the form does not affect eCTD or NeeS/VNeeS validation - the purpose of the form validation is simply to guide you to fill in the form correctly and to fill in mandatory fields of the forms.
- In many cases, form validation errors do not lead business validation errors.
- Form that doesn't have any form validation errors might still be invalidated during the business validation step – it's important not to confuse form validation with business content validation!
- If a new version of the forms has become available / entered into force between the receipt of a new (initial, variation or renewal) application and request for supplementary information (validation comments) or the finalisation of the regulatory activity - the applicant **does not** need to change the form version!

How to lock the form (1)



- After finalising data entry you will need to lock the form before submitting it to the authorities
- Save the un-locked form in advance, you may need to change data at a later point in time
- Navigate to section 'Signature'
- The tool tip describes the actions required
- Select an image from file system
- Before the form is locked a validation process is running and will indicate all missing values
- This process cannot be stopped*
- Once the process ends all fields are displayed in grey, the validation error sum will be displayed at the far end of the form

Function	<input type="text"/>
Address 1	Kurt-Georg-Kiesinger-Allee 3
Address 2	<input type="text"/>
Postcode	53175
Country	Germany
Telephone	+49 228 207 3
Telefax	<input type="text"/>
E-mail	klaus.menges@bfarm.de
Date	<input type="text"/>
Signatory	Validating Form - Please Wait

In process once the signature image has been added and saving the file was confirmed

This form was authorised following company policies by Dr. K. Menges, Senior Reg. Affairs Manager of BfArM with authorisation to sign. The signature is in file.

- Note: please attach letter of authorisation for communication/signing on behalf of the applicant in (Annex 5.4)
- Note: if fees have been paid, attach proof of payment in (Annex 5.1) - see information on fee payments on EMA/CMD

FORM VALIDATION

Validation Errors: 0



- Once the form has been saved and is locked the presentation changes to grey
- The image could be an image of a real signature as well

On behalf of the applicant

Title

First name* Klaus

Surname Menges

Function

Address 1 Kurt-Georg-Kiesinger-Allee 3

Address 2

Postcode 53175

Country Germany

Telephone +49 228 207 3458

Telefax

E-mail klaus.menges@bfarm.de

Date

Signatory



* Note: please attach letter of authorisation for communication/signing on behalf of the applicant in (Annex 5.4)

** Note: if fees have been paid, attach proof of payment : (Annex 5.1) see information on fee payments on EMA/CMDh website.

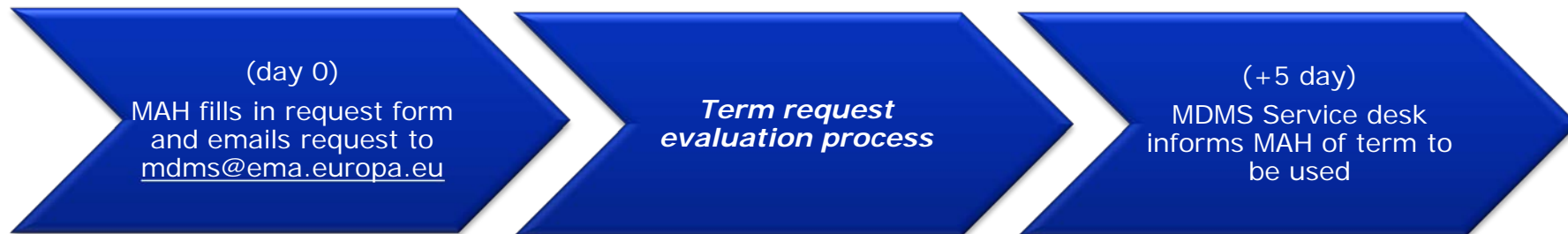


- The dropdown lists or selections from catalogues include terms according to standardised nomenclatures and quality standards for medicinal substances and products of EDQM or the EUTCT system
- In case of a missing term please use the [eAF Term Request Form](#). Once completed, you will need to submit your form via email to mdms@ema.europa.eu
- A provisional term may be added to the list within 5 working days; however, please note that there is a possibility that the term might not be approved and ultimately added to the list for future use. For further guidance please refer to http://esubmission.ema.europa.eu/eaf/5_eAF%20Term%20Request%20Process.ppt
- In case NCAs identify that an inappropriate term has been used, the applicant must correct it and should ask for a provisional term according to the defined process
- All controlled terminology lists used in the eAF can be found from EUTCT
- Initial testing shows that it is possible to copy content selected from dropdown menus in v.1.19 – this might depend on the version of Adobe you have available



In case MAH/NCA will ask for new terms

→ EMA provides a standardised request procedure available on the eAF website



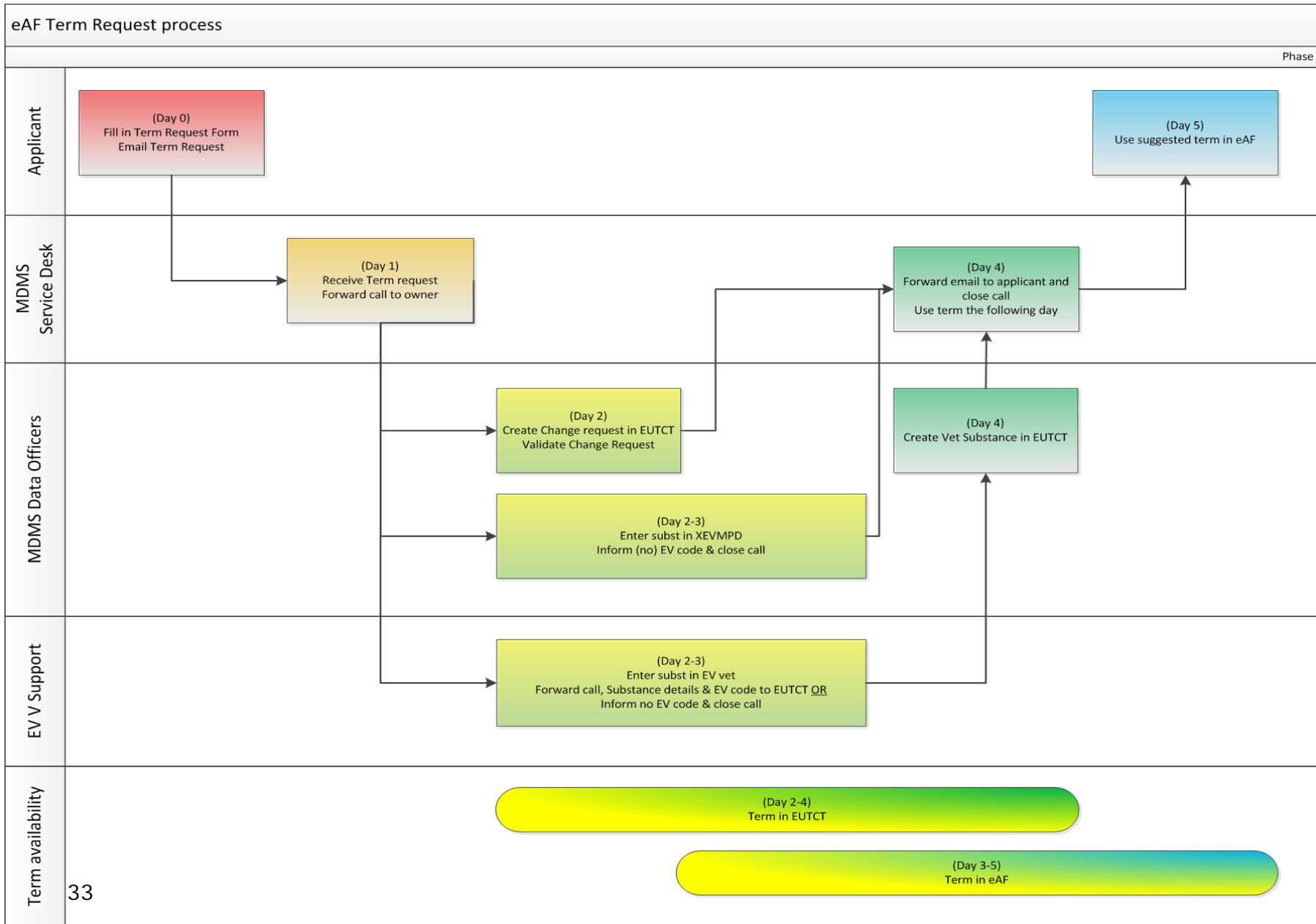
** In the term request form there are detailed instructions on what information is required to apply for changes in each list.*

Note: Sending term requests to eAF@ema.europa.eu may cause delays in handling your request – the requests for any new terminology or changes in EUTCT should always be sent to mdms@ema.europa.eu

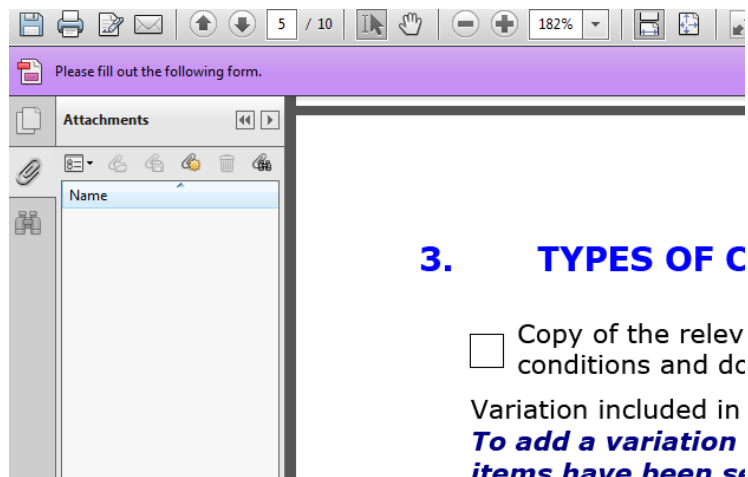
eAF Term Request Process – 5 days SLA



EUROPEAN MEDICINES AGENCY



- The most commonly used workaround solution is an addition of an annex to the form as the relevant section cannot be filled as required in the eAF - these are not the annexes as referred to e.g. in section 5 of the initial forms
- The annex must be included as a separate, **clearly named** document in the same folder (e.g. 1.2 in EU M1) where the application form is provided! We recommend that the annex is named as per the section of the form that is provided in the annex (e.g. Annex 2.6.1).
- The standard PDF functionality of adding an annex using the paperclip function must not be used as the annexed documents will not be visible when viewed via eCTD review tool (e.g. EURS)



ANNEXED DOCUMENTS (WHERE APPROPRIATE)

The following amended product information proposals are provided in volume 6B format, where applicable:

- Summary of product characteristics
- Manufacturing Authorisation Holder responsible for batch release
- Labelling
- Package leaflet



- For MRP/DCP the renewal form might contain multiple product names all entered in the same single row as the current version of the form does not allow duplication of the 'Invented name' field.

Is the product currently marketed? Yes No

In which Member States²? 

Member state	Germany	<input data-bbox="1207 582 1277 639" type="button" value="+"/>	<input data-bbox="1277 582 1354 639" type="button" value="-"/>
Member state	Finland	<input data-bbox="1207 689 1277 746" type="button" value="+"/>	<input data-bbox="1277 689 1354 746" type="button" value="-"/>

Invented Name DE: Product A, FI: Product B, BE: Product C

- There is an existing change request based on feedback from NCAs that this is a field that is duplicated in the paper forms. This change will be implemented in the eAF v. 1.20.



- For MRP/DCP the **variation form** will cover multiple product names by using the Annex B option or you may enter multiple product names already here and details in the annex.
- You need to enter the high level number in section 1 or **DE/H/5555/001-003/1A/018/G** in case of worksharing, where to include the product specific variation number **AT/H/xxxx/001G**
- You should also enter the MRP number and the national authorisation number before using the Annex B option to allow a proper identification of the product out of the XML data set.
- Repeat the lower section as needed.

2. PRODUCTS CONCERNED BY THIS APPLICATION⁷

(Invented) Name **see Annex B**

Pharmaceutical Form:

Strength: Units

Active Substance

MRP Variation Number⁸ **DE/H/5555/001-003/1A/018/G**

Member States **Belgium**

MA Holder Name **see Annex B**

MA Number⁸ **BE67895**

Clear Annex B



- Duplicating the entire section should only be used in case products are concerned which differ in regard to pharmaceutical form and active ingredients.
- If different product names need to be covered the previous workaround is easier to handle.
- Entering the correct MRP number is again essential to allow a proper identification of the product out of the XML data set.

2. PRODUCTS CONCERNED BY THIS APPLICATION⁷

The screenshot displays the 'PRODUCTS CONCERNED BY THIS APPLICATION' section of the eAF interface. It is divided into two main panels. The top panel, highlighted with a blue border, contains fields for '(Invented) Name', 'Pharmaceutical Form', 'Strength', 'Units', and 'Active Substance'. Each field has associated '+' and '-' buttons for duplication. The bottom panel, highlighted with a green border, contains the 'MRP Variation Number⁸' field (containing 'AT/H/0234/001/IA/001/G'), 'Member States', 'MA Holder Name', and 'MA Number⁸' (containing 'AT67895'). Information icons (i) are present next to the 'MRP Variation Number' and 'MA Number' labels. At the bottom of the interface are buttons for 'OK', 'Clear', 'Cancel', 'see Annex A', and 'see Annex B'. A blue arrow points to a '+' button in the top right of the first panel, and two green arrows point to the 'MRP Variation Number' and 'MA Number' fields in the second panel.



- Duplicating the entire section should only be used in case products are concerned which differ in regard to pharmaceutical form and active substance.
- If different products need to be covered by previous workarounds, it is easier to handle.
- Entering the correct MA number is again necessary to allow a proper identification of the product out of the XML data set.

2. PRODUCTS CONCERNED BY THIS APPLICATION⁷ ⓘ

(Invented) Name

Pharmaceutical Form

Member States

MA Holder Name

MA Number⁸ ⓘ

[see Annex A](#) [see Annex B](#)

However, this workaround is complex and still not ideal. It will also not support all needs. That's why we are working on an improvement for release 1.20. This is planned for testing in March / April 2016.



- Detailed instructions how to use workaround solutions is available in the [eAF Q&A document](#) and the [eAF Technical Guidance](#) documents – both are published on the eAF webpage – if you need more advice contact eAF@ema.europa.eu.
- If you have a question that is not responded to in the guidance documents send your question to eAF@ema.europa.eu. Most commonly asked questions will be added in to the Q&A document and in the eAF Technical Guidance document during the next update of these documents.
- The forms have been built so that they contain build in business rules, guiding you to fill in the forms the correct way and this might in some sections compromise flexibility, however, the forms remain flexible and there are multiple different ways to fill in several sections depending on each specific application. EMA directs applicants to NCAs/RMS when there are questions on how to fill in certain parts of the forms for MRP/DCP/NP applications to ensure there are no content validation issues.



- Applicants should always mention in the application cover letter that a workaround solution has been used to avoid any business validation issues. There is no need to mention the workaround for addition of the salt/hydrate form as this is not displayed as a workaround for NCAs.
- The current version of the forms has some known defects and issues for which an updated 'known defects and workaround solutions document' will be made available on the eSubmission website.
- Some of the known defects in the forms released on 9th November 2015 were severe and an emergency hotfix was released on Monday 30th November 2015 – the date from when the v1.19 will replace v1.18 has been postponed until 11th January 2016 – the date of the mandatory use of the eAF has not been postponed!
- Version 1.19.01 becomes mandatory to use after 11th January 2016.



- v1.19 of the variation eAF is duplicating fields in Section 2 Products Concerned By This Application, if a second Invented Name for an MRP submission is added the form adds a second section, but also adds fields for MA Holder Name and MA Number in two places, not replicating the structure of the original section (see screenshots below and attached eAF). This issue is persisting also when 'National authorisation' selected. For national variations the MRP field should be ignored.

Active Substance(s):
LINEZOLID

Add Active Substance(s)

MA Holder Name Pfizer B

MA Number^a 56789

MRP Variation Number^a
123456

Member States Austria

MA Holder Name Pfizer B

MA Number^a 56789

see Annex A see Annex B



- v1.19 of the variation eAF is not displaying the name of the certain z scopes correctly in the summary box and in the 'present and proposed' section. This is a very complex defect and hence there is no immediate fix provided for the variation form as part of the hotfix. Please provide the details in the precise scope field and describe the issue on the cover letter.

Variation	Selected
z)	2
B.I.e.3	1
B.I.e.2	1

		Procedu
<input checked="" type="checkbox"/> B.I.e.2	Introduction of a post approval change management protocol related to the active substance	II
<input checked="" type="checkbox"/> z)	Other variation	<input checked="" type="checkbox"/> IA <input type="checkbox"/>

- The location of the eAF within the dossier does not change due to the change to eAF
- You may use the same file names as in the past
- Due to a possibly higher number of attached annexes it is highly recommend to follow this naming convention (extending the usage of the variable part):
 - eCTD and NeesS: **cc-form-eaf-var.pdf** will contain the eAF PDF file, XML data will be extracted from there. If any additional file is named differently it will become very easy for NCAs to identify the file to be extracted

All annexed files should make use of the variable part to identify different content, e.g. annex on section 2.6.2 or proof of payment or annex 5.19:

cc-form-annex2-6-2.pdf, **cc-form-proofpayment.pdf** , **cc-form-annex-5-19.pdf**

- **In MRP/DCP one common application form is highly recommended, one per pharmaceutical form or strength for all member states in case of new MAA and one eAF for all involved products for all member states in case of variations and renewals.**
- VNeesS: As there no detailed naming convention exists it is recommended to adapt the file names as it is required for human medicinal products



- Data can be extracted from the PDF file in XML format at any time
- If the form has been 'locked', neither the applicant nor the receiving agency is able to make changes to the form. However, the marked buttons at the far end of the form are still working

```
<?xml version="1.0" encoding="UTF-8" standalone="no" ?>
<xfa:data xmlns:xfa="http://www.xfa.org/schema/xfa-data/1.0/">
  <maa:eu_application_form xsi:schemaLocation="http://www.ema.eaf/maa/maa_human.xsd"
    xmlns:xsi="http://www.w3.org/2001/XMLSchemainstance" xmlns:rdm="http://www.ema.eaf/dictionary/"
    xmlns:maa="http://www.ema.eaf/maa/">
    <maa:envelope>...</maa:envelope>
    <maa:initial-application-form-human>
      <maa:scientific-advice>...</maa:scientific-advice>
      <maa:declaration>...</maa:declaration>
      <maa:chapter-1>
        <maa:procedure-type>
          <maa:centralised-procedure>...</maa:centralised-procedure>
          <maa:mutual-recognition-procedure>
            <rdm:selected>1</rdm:selected>
            <rdm:selected_scope></rdm:selected_scope>
            <rdm:procedure-number>DE/H/1234/001/MR</rdm:procedure-number>
            <rdm:reference-member-state>100000000403|Germany</rdm:reference-member-state>
            <rdm:date-of-authorisation>2014-02-26</rdm:date-of-authorisation>
            <rdm:market-authorisation-number>12345.00.00</rdm:market-authorisation-number>
            <rdm:first-use>1</rdm:first-use>
            <rdm:waiver-amendment-psur></rdm:waiver-amendment-psur>
            <rdm:member-renewals>...</rdm:member-renewals>
          </maa:mutual-recognition-procedure>
          <maa:decentralised-procedure>...</maa:decentralised-procedure>
          <maa:national-procedure>...</maa:national-procedure>
        </maa:procedure-type>
      </maa:chapter-1>
    </maa:initial-application-form-human>
  </maa:eu_application_form>
</xfa:data>
```





- Slide 47 to 48 – Form versions
- Slide 49 – Guidance
- Slide 50 – Locking and signature
- Slide 51 to 56 – MRP/DCP
- Slide 57 to 59 – National requirements
- Slide 60 – Paper submissions
- Slide 61 – Templates
- Slide 62 to 67 – Variations specific
- Slide 68 to 69 – Renewal Form
- Slide 70 to 77 – Initial MAA form
- Slide 78 – Veterinary specifics
- Slide 79 – Missing terminology
- Slide 80 – Form validation errors
- Slide 81 – Salt/Hydrate form
- Slide 82 – Fast web view
- Slide 83 – Web services
- Slide 83 to 89 – Issues
- Slide 90 – Urgent help
- Slide 71 – Submissions
- Slide 92 – NeeS submissions
- Slide 93 – Change requests



- Will applicants be informed of upcoming updates to the AF some time in advance of it coming into force?

Yes, please check eAF - website

- If so, how long in advance?

The release schedule is available in the eAF webpage. For example; the date for version 1.20 has been published (15.04.2015)

- What if we have prepared a variation with the electronic AF and while finalising all the documentation for the submission there is an update to the AF (a new version). For how long will the previous version be accepted for submission?

A transitional period is available – please find details for version 1.20 in this presentation.

- Will there be a technical possibility to update the AF to the new version without losing the variation/product/company specific data added?

It is possible to export and import the user inserted data to the new version of the form, however, updates of the underlying data exchange standard (XML-data) can mean that some fields are not correctly imported.

Normally usability changes will have no impact on the data imports, however, e.g. v. 01.20 will change the DES



- Is it possible to use current AF (paper version) within the eCTD for the MAAs submitted till 31.12.2015 till the end of the procedure? Namely, if there is a change impacting AF during the procedure, it would be a double work (first filling out paper version and then complete eAF from the scratch). Also, some MSs could have comment on eAF whereas not having them till that moment on paper version of the AF?

There is no need to change the format or the version of the application in the middle of the procedure.

- Is it expected with eAF becoming mandatory 1/1/16, that already approved paper AF needs to be converted to eAF, when submitting a baseline sequence next year to start eCTD lifecycle?

When the baseline is provided with a **new** regulatory activity it should contain the latest version of the eAF. It is now mandatory to use the eAFs for all human and veterinary initial, variation and renewal applications.

- We have understood that it is not required to change from a paper application form to the eAF, but our question is this: is it permissible to change to an eAF mid-procedure should one wish to do so?

It is not recommended to change the format of the form in the middle of the procedure. For compelling reasons please contact the RMS, relevant NCA or the EMA for confirmation of acceptability of the format change in the middle the procedure.



- Will the guidance and Q&A documents be updated before end of the year, when?

Regular updates are planned and next update is expected in January 2016.



- Will the process to lock the form be changed (currently import of a signature image needed), e.g. by a button or tick box?

There are no existing CRs or other plans to change this functionality.

- What does this mean regarding the legal relevance of the signature image and what is required to authorise the form by the MAH from a legal perspective?

“This image will not work as a digital advanced or qualified electronic signature nor can replace requirements of wet signed forms.”

Please check national requirements for signatures.

- Does the scanned image work as a digital advanced or qualified electronic signature? Can it replace requirements of wet signed forms?

Please check national requirements for signatures.

- We know that a qualified certificate is needed to sign EMA forms. Therefore we take into account as an option to use SAFE BioPharma certificates. But I’m unsure if they fulfill the EMA requirements. I saw that there is a list of TrustCenters, but I don’t find no non-country-specific providers. Where can I check if we are able to use SAFE for EMA submissions?

The forms should be signed using a scanned image of a signature. There is no need to use qualified signatures for eAFs submitted to the EMA for Centralised Procedure applications.



- Should we use one single (common) form for all Member States in the MRP/DCP applications?

Yes, this is highly recommended. There are no country specific electronic application forms available.

- Is one single (common) form in English language accepted?

Yes, there are no national translations available; in MRP/DCP all member states should accept the application form in common language. Please consult CMDh and CMDv web-sites.

- Are additional paper forms (with wet-ink signature) required in any Member State?

Please check national requirements; harmonisation of the signature requirements is not in the remit of the eAF MG. Questions on national requirements should be forwarded directly to the relevant NCA.



- Can we submit a common and unique e-AF for MRP/DCP? How will it be managed?

Yes, this is highly recommended.

New MAA: one eAF per pharmaceutical form or strength for all member states

Variations and renewals: one eAF for all involved products for all member states

The file name will be **common-form-var.pdf**, the variable part should be used as outlined in the file & folder naming convention of the updated validation criteria version 6.0. This new version will be published very soon.

Recommended usage of the variable part of the file name in this section:

cc-form-eaf-var.pdf

cc-form-annex-var.pdf

- For MRP/DCP procedures, how many e-AFs should be included in the dossier? If one single AF is required, who is the signatory?

The number of forms will depend from the regulatory activity as outlined before. The signature should be provided by the responsible MAH or can be provided by any authorised deputy.



- A question regarding 1 common eAF in the sequence for DCP procedures which was mentioned on the EMA webinar in December. We have procedures with different MAH and contact persons for relevant CMSs. Currently, person for each MAH sign the application form which is then placed in the sequence. So we have many application forms in the sequence, same information but signed by different person. It is not clear how we can handle this process now and who can sign the one common application form. Signature is based on power of attorney according to CMSs requirements?
The new MAA form is required per form or strength, but should be a common one for all member states involved. The signature can be included by the applicant or any authorised representative. The current policy will not change by using eAFs. The variation form allows to include all forms and strengths. Again, the signatures should be provided by the MAH. If different national companies are involved it is recommended to add power of attorney as required by member states appropriately.



- We use a specific AF for Homeopathic medicinal products' Marketing Authorisation Applications. Will a specific eAF be published and when?

This specific form is currently not adapted to an eAF. It needs to be clarified whether existing differences and additional needs can be accommodated in the eAF MAA (hum and vet).

- Use of eCTD is not mandatory in the NCA to which I'm submitting to. Do I still have to use the eAF?

Yes, the use of eAF is now mandatory for all submission formats including paper based applications.

- Will each National Competent Authority decide whether the eAF should be compulsory or not for National?

The NTA application forms have been replaced by the eAFs for all procedure types. If you have any questions, please contact the relevant NCA.



- In DCP/MRP an AF signed by multiple responsible persons is needed for communication with specific Authorities (could be initial submission or renewal or variation). How this can be done with 1 AF? Or it is possible only with multiple AFs where only signatory person is different?

Ideally provide a single contact point. For those NCAs that require multiple contact persons include a separate annex with the contact details.

- Using a single eAF for MRPs/DCPs for all member states: In particular, information on Section 1, Name and address of the Applicant/MA holder – within an MRP/DCP submission, the Application/MA holder may differ per member state. This section is currently not replicable, therefore we are unable to add differing Applicants/MA holders within one single form. We suggest making the applicant section of the eAF repeatable.

This is an existing change request to the form and we are hoping to improve this section in the next release of the forms (v. 01.20)



- In an MRP variation, is the attachment to eAF, “list of concerned products” the best way to show multiple invented names in section “2. Products concerned with this application”? If we add several “2. Products concerned...” sections, the information regarding MA holder and MA number appear multiple times?

The section 2 of the variation form will completely change in the next release of the variation eAF planned for April 2016. The new layout will significantly improve the usability of this section and will make it easier to use for MRP/DCP applications.

For workaround solution in the current version, please see slide 36. In summary: prior to release 1.20 use of annex ‘list of concerned products’ is possible to show different invented names. Different invented names could also be listed in the field ‘Invented name’ of the form with indication of the name in each relevant NCA as shown below in the screenshot:

2. PRODUCTS CONCERNED BY THIS APPLICATION⁷ ⓘ

(Invented) Name	DE, UK, IE: Wonderpill FI, SE, DK, NO: Superpill	+ -
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- Will the national requirements for local language form requirements remain, and if so, what is the suggested workaround for this.

Please contact the relevant NCA. There are different approaches available. eAF forms are only available in English.

- Can you confirm that there is no requirement for national translations of the eAF in any procedure type.

Yes, it is highly recommended to provide a common form in common language. NCAs are required to accept the common version of the form. At the moment, we cannot exclude that some NCA require an additional document / translation in the workingdocuments folder or via a portal

- eAF will become mandatory for all types of licenses (Human) on 01-Jan-2016. Is there any visibility on whether national authorities will continue to require filling in a specific form linked to their own database (for example in Spain, currently the Application Forms are generated by the authorities database, with additional requirements and validation steps than those present in the eAF)

Please contact the relevant NCA; send feedback to eaf@ema.europa.eu



- Currently they are countries which are requesting originally signed AFs (without national translation required), to be submitted (irrespective if the submission is done via CESP or not). Will this be still necessary? If yes, the unsigned eAF will be printed, signed and submitted?

The eAF does not change the wet signature requirements at the NCAs. Please check the national requirements for wet signatures to avoid validation issues.

- What format of AF should I submit in Countries where originally signed AF in paper format is required according to national requirements?

Please contact the relevant NCA whether there is a need for a wet signed form in parallel. Scanned eAF are invalid and will be rejected. The unsigned eAF can be printed, signed and submitted as per the NCA requirements.

- National wet signed Application Form requirements. We understand that the requirement for wet signed copies of the Application Form will remain. Following communication with the EMA, we have proposed the provision of printed versions of the eAF countersigned in ink, however, some countries have requested that a PDF scan of the wet signed version be included within the eCTD/NeeS. We question the requirement and value in providing this as the eAF and wet signed requirements will have been met.

This issue will be communicated to CMDh and CMDv because it cannot be solved within eAF MG.



•To what extent does country-specific information have to be included in the eAF? For some information (e.g. for MAH, MA number) provision is made for, but national particulars cannot be entered for other data (e.g. invented name, proof of payment, contact info). This seems to be an inconsistent approach which makes it difficult for companies to decide on a clear internal strategy. It can also lead to slightly different application forms in the concerned member states. Thus it would be helpful to have some room to move (e.g. extend the “see annex A/B” workaround also to other sections and not just use it for MAH, MA number). It would also be interesting to hear how other companies deal with country-specific information, and what authorities actually expect.

It is recommended to prepare additional annexes, if the form does not provide sufficient possibilities itself. Annexes based on section 5 can be indicated in the respective section and need to be added in Module 1.2 anyway. A naming convention is recommended and will be added to the validation criteria. Due to the high variability of needs, this will not be added to become P/F.

For any proposals for improvements in the future forms, please submit a change request to eAF@ema.europa.eu with detailed suggestions how to improve the forms. Please include simple mock-ups of the proposed design and functionality.



- I am still submitting in paper should I prepare the eAF to send to the agency electronically in parallel and then print it to go with the paper? eAF will completely replace the NTA application forms. Please check national submission requirements if parallel electronic submission is required. The eAF can be printed and signed for paper submissions.

- I have seen some colleagues who are already preparing the eAF but after completion they will print the form to sign and scan it to be included in the submission. What suggestion is there to get around the electronic version of their signature, which is required to validate the form?

Printing and scanning the signed form should only be done for paper submissions as this way the eAF will become a flat PDF. EMA will reject all flat PDF application forms.



- Would the EMA agree that a master form can be prepared containing general entries that will not change, which can be 'Saved As' each time. This would remove the need for the author to update each of the drop downs etc. each time they need to complete the form? Only the details relating to the current submission would be required i.e. application number, description etc?

It is recommended that a template is created by the MAHs/applicants that can be used over and over again without a need to refill all the information. It is however very important to observe if new versions of the forms become available. In those cases the templates will need to be updated.



- In the variations eAF it is possible to select the types of change(s)/variation categories. Nevertheless the relevant page(s) from the Guideline for this/these change(s) still need to be attached and the relevant boxes for conditions and documentation (both for Type IA and Type IB) need to be ticked. Are there any plans to integrate this into the eAF? Any timelines available?

There is an existing change request to improve the variations form. The proposed change is however a major change to the variation form and it is likely that this will not be implemented before the introduction of the Single Submission Portal

- For variation AF how the Classification Guideline table will be added?

The classification Guideline table should be added as a separate document annexed to the application form. It should be provided in the same folder as the application form, clearly named as Classification Guideline

- eAF doesn't contain the condition(s) to which variation has to comply and documentation(s) which has to be submitted acc to type of variation. How can be this part added to the variation form?

The conditions should be provided as a separate document annexed to the application form. It should be provided in the same folder as the application form, clearly named as Classification Guideline. It is important not to attach the annexes in to the eAF itself, this will prevent proper locking of the forms.



- How to represent deleted text in eAF, as strikethrough option is not available
In the section of present/proposed text in the variation form it is possible to paste in text with strike through formatted characters using RTF.

PRESENT ^{9,10}	PROPOSED ^{9,10}	i
Hinweise <ul style="list-style-type: none">• Bislang sind keine weiteren Dokumente, die in der Sitzung verwendet werden könnten (z B. aktuelles Bild der Systemlandschaft) eingetragen	Hinweise <ul style="list-style-type: none">• Bislang sind keine weiteren Dokumente, die in der Sitzung verwendet werden könnten (z B. aktuelles Bild der Systemlandschaft) eingetragen	+ -



- Section 1: Why does “variation procedure number” becomes visible when choosing national procedure? This is not applicable for national procedures
Purely national variation procedures will not use the MRP procedure number. However a procedure number may exist for national procedures and it may be used as a tracking number. The data field will offer a place for it. An information note may be added to the form to not confuse people.
- Section 2: For national procedures the set-up for MA holder name and MA number is not including Member state. The only section for national procedures where member state is present is in the section 1 “Name and address of contact person”. Why is it not aligned with the same set-up as for National Authorisation in MRP/DCP?
This deficiency will be managed with in the next version. currently a workaround (additional annex) is required.

PROPOSED ^{9,10}	
<u>Notizen</u>	
text	result
text	result 2
text	result 3
text	result 4
text	result 1
text	result 2
text	result 3
text	result 4

- Section 3: “Scope and background” and “Present and proposed”: Will it become possible to insert a table? It would create a better overview and ease the readability
Currently you can use text lines and insert blanks to structure the layout similarly; a CR will be discussed
- Will it become possible to integrate the dossier requirements into the eAF for variations?
To be responded in writing. More details on the request required.

Variation application form / Formatting within present-proposed table:

•How can we fill the present propose-table in a more effective way?

•Concerns: The fact that no table-formatted content can be added in the text fields, forces the users to add screenshots instead; which is a tedious and time-consuming task (no copy-paste can be done, each screenshot needs to be saved as a file before being included in the image field). In addition this approach is not user friendly, since no further edits are possible and also the image could be of bad quality and low readability. In addition, the image fields are not adapting to the size of the images included, which means that the screenshots have to match with the size of the field (200 pixels of height) to be readable. This adds to the complexity as many screenshots have to be created to cover big tables.

More complex descriptions can be provided in an separate annex to the eAF. This annex should be clearly named and should be provided in the same folder as the application form within the submission package.

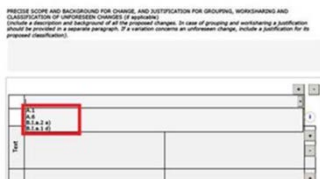
•How can we add table-formatted data in the present-proposed table? [see previous question](#)

How can we copy-paste an Image? [You can select an image from the file system per each cell](#)

How can we add multiple pictures in the same image field? [Just one image per cell should be included. The cells are repeatable.](#)

How can we adapt the picture to the size of the field ? [The image cannot be enlarged. If the size needs to be adjusted please provide the image as an annex.](#)

How can we alternate text fields and image fields in the present-proposed-table (e.g. text-image-text-image-text)? [It is not possible within one section of the present/proposed table. You will need to repeat the section entirely.](#)



•Variation drop-down for present-proposed table:

How can we select multiple variations for one section of the present-proposed table (e.g. several changes might be located in the same section of a document)? [There is only one reference option provided.](#)

•How can we reflect “Editorial Changes” in the present-proposed table and which drop-down option we choose for this type of changes?

[Editorial changes should be described in the present-proposed table, but are not necessarily directly related to a variation editorial changes.](#)



Variation application form / Formatting within present-proposed table:

- **Copy of the relevant pages from the Guideline** :/ How can we provide the copy of the relevant pages from the Guideline?

3. TYPES OF CHANGE(S)

Copy of the relevant page(s) from the Guideline for this/these change(s) is at conditions and documentation (both for Type IA and Type IB) are ticked.

- In situations that require an extensive explanation in a specific comment field, how can we proceed if we do not have enough space for our clarifications (e.g. some comment fields only accept 50 characters)?

More complex descriptions and copies of the relevant conditions need be provided in an annex.

- Can you make this a future improvement that the copy of the relevant page guideline will automatically be attached as annex to the AF?

This is an existing change request, however this is a very complex CR which is unlikely to be done prior to the single submission portal version.



- We have a variation concerning a product family with three products: tablets, suspension, and a combination package of the two pharmaceutical forms that contains both tablets and suspension. How to best show this combination product in the eAF when there is no “combination product” in the pharmaceutical forms pick list?

In case of the combination pack you have to repeat the product section and to include two pharmaceutical forms. You will enter the active ingredient two times, but may be this differs in the two forms as well.

- regarding the eAF for Variations we struggled with section 3 / Type of changes in case of a CI4z which displays as follows:

The screenshot shows a software interface for entering variation data. At the top, there are two buttons: "Show All Types" and "Refresh Selected". Below these is a table with two columns: "Variation" and "Selected". The first row contains "z)" and "1".

Variation	Selected
z)	1

Below this table is a larger form area. On the left, there is a table with a checkbox and a variation type:

<input checked="" type="checkbox"/> z)	Other variation
--	-----------------

To the right of this table is a "Procedure type" section with three radio buttons: IA, IB, and II. Further right, there is a section for "Art. 5" with a checkbox, and "Implement. Date:" with two empty input fields. To the right of the date fields are two small buttons, "+" and "-".

- If you want to show that it is C.I.4.z you end up with ticking 2 lines as shown below (which could be understood as applying for 2 variations instead of 1) and the C.I.4 line displays a Type II variation, which is not correct

This is a known defect in the variation form which we are trying to solve in the version 1.20. Meanwhile a workaround solution will need to be used by adding the details of the scope in the field 'precise scope and background for change' and addressing this issue in the cover letter.



- Section 1: section for MA numbers: only the CMS countries are listed – shouldn't the RMS be listed as well? How do we fill in the MA number for the RMS?

If you select MRP the additional lines for RMS and procedure number will be displayed. This was a known defect that has now been fixed in the release 01.19.0.1 released on 30th November 2015.

- Section 2: Active substance manufacturers: it is not possible to add a function of the manufacturer – how do you discriminate between e.g. manufacturers of intermediates for API and the actual API manufacturer?

You can describe the role of the manufacturer in the first line. The section can be repeated as often as needed.

2. APPROVED MANUFACTURERS

Authorised manufacturer(s) (or importer) responsible for **batch release** in the EEA (in accordance with Articles 40 and 51 of Directive 2001/83/EC, as amended, or Articles 44 and 55 of Directive 2001/82/EC (as shown in the package leaflet and where applicable in the labelling or Annex II of the Decision))



•Composition: How do you fill in details for an excipient that has been approved with the amount "q.s."?

Q.S was introduced as quantity operator in the eAFs and will now allow to describe the limits precisely. The guidance will be updated to reflect this change.

Name of active substance	Quantity / Unit
<input type="text"/>	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>
	<input type="text"/> <input type="text"/>

approximately equal to
equal to
equivalent to
less than
less than or equal to
more than
more than or equal to
quantity sufficient
range

•Renewal form – revision June 2015; Is there some kind of overview which explains all abbreviations used in the drop down list. For example, at section 1, when you need to complete the composition of the active substances for a tablet, you cannot choose xx mg/tablet. There is the possibility of mg/U, but I'm not sure what the "U" stands for, is it unit?

Values are re-used from EUTCT. Details can be retrieved from term details. In general, the abbreviations should follow common standards, i.e. The International System of Units



- In section, 2.6.1 Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s) there is no space to include a note to the Qualitative and Quantitative composition after the excipients list.

At the moment you have an option to add a note above of each list.

The screenshot shows a software interface for the MAA form. At the top, there is a text box containing the text: "In section, 2.6.1 Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s) there is no space to include a note to the Quali". Below this text box is a table with three columns: "Name of Excipient", "Quantity / Unit", and "Reference / Monograph Standard". There are plus and minus buttons in the top right corner of the text box and a plus button in the bottom right corner of the table.

Name of Excipient	Quantity / Unit	Reference / Monograph Standard
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- For the section 2.4.4 Summary of the pharmacovigilance system, in a community procedure with more than 1 MAH the section "Qualified Person in EEA for Pharmacovigilance " can be multiplied for more than one QPPV, but the location of the Pharmacovigilance system master file is only one section and cannot be multiplied as to indicate all locations per each pharmacovigilance system. Which location should be described here?

In this case section 2.4.4 needs to be repeated as different PV master files will be maintained. For each system the QPPV may be identical.



• Person authorised for communication*, on behalf of the Applicant and Section 2.4.2 of the application form. We as generic company intend to submit MAA from India on EU based MAH in Europe. Till date, all the regulatory activities are managed by India office only wherein EU based MAH will provide the LOA to the responsible person for communication during the procedure. So we would to have a provision for the person who communicates on behalf of applicant from India. In the eAF for the section “Person authorised for communication*, on behalf of the Applicant” the country India is not listed in the drop down list?

As a workaround solution you can enter the country name in the ‘Address 2’ field after the city/town element and leave the ‘country’ field empty. Please ignore the form validation error and mention this in the cover letter. This has been raised as a new change request for a future release of the form.

• Section 2.4.1 of application form. We are unable to activate any of the option in the section 2.4.1 i.e. Centralised procedure/National procedure including MRP/DCP. Both the options are frozen?

This was a known defect in form version 1.19.00 and has been fixed in the hotfix release (1.19.01) on 30 November 2015. It is mandatory to use the v. 1.19.01 after 11th January 2016.



- Section 2.4.4 Qualified person in the EEA for Pharmacovigilance:

Kindly note that as per national requirements for some of the NCAs (example Portugal & Spain) a local contact person for Pharmacovigilance has to be mentioned in section 2.4.4. Please let us know how to proceed in this case. Absence of local PV details will leads to validation issues

This section can be repeated and the specific details can be added. All NCAs have agreed to the use of the eAF from 1 January 2016. For any additional national requirements, you can attach an annex to the form. Place the annex in the same folder as the eAF (EU M1, section 1.2) and name it clearly Annex section 2.4.4.

- Please also note that once the application form is locked, the drop down list is still functioning

Once the form is locked all dropdown menus should also be locked.

Please provide the copy of the form to eAF@ema.europa.eu with details of the issue for investigation.



•Section 2.5.3 Manufacturer(s) of the active substance(s) and site(s) of manufacture? Kindly note that if my active substance holds a CEP certificate then we don't find the option for Annex 5.11 in this section. Is Annex 5.11 not required if the active substance has CEP

We understand, that the form is completed here and annex 5.10 will be referenced.

Has a Ph.Eur. Certificate of suitability been issued for the active substance(s):

Yes No

Name of the CEP holder

Name of the manufacturer if different from the above

CEP number

Date of last update

Provide copy in [\(Annex 5.10\)](#)

The checkbox for annex 5.11 is currently explicitly displayed only when ASMF is ticked. This needs to be changed in the next version.

Attach copy of confirmation from the manufacturer of the active substance to inform the applicant in case of modification of the manufacturing process or specifications according to Annex 1 of Directive 2001/82/EC [\(Annex 5.11\)](#)

As a workaround, you can tick ASMF and then the annex 5.11 checkbox. If you deselect ASMF, the annex 5.11 button remains ticked in section 5 and no validation error will be created.

Questions – Initial MAA form



- Regarding the eAF for initial MA application: Section 1.3 for the legal basis cannot be completed (the boxes which should normally be ticked (e.g. 1.3.1 for Art. 12(3)) do not pop up);

For the GMP-related information (5.9 and 5.10), there is a technical mismatch between the information ticked in the eAF and the automatic ticked boxes in the Annex to the eAF

Thank you for reporting this issue. The eAF helpdesk will look into these technical issues and will deploy defect fixes in future releases. You will receive direct communication from eAF helpdesk in near future.

- Section 2.5.1a Batch release:

There is empty field: what is necessary to write here? Why is there information about packaging in help window? If I have different/multiple manufacturers responsible for batch release I can use + and add it

The free text field is included so that those applicants who have multiple packaging can include details of which packaging the manufacturer is responsible for i.e. to show the relationship between the packaging and the manufacturer. This is an optional field that can be left empty it is not needed.

2.5 MANUFACTURERS
Note: ALL manufacturing and control sites mentioned throughout the whole dossier MUST be consistent regarding their names, detailed addresses and activities.

2.5.1 a Authorised manufacturer(s) (or importer(s)) responsible for batch release in the EEA in accordance with Article 40 and Article 51 of Directive 2001/83/EC (as shown in the package leaflet and where applicable in the labelling or Annex: II of the Commission Decision):

+ -	
[Empty text field]	
Do you have a separate address for each manufacturer? <input type="radio"/> Yes <input type="radio"/> No	
[Free text field for packaging details]	
Company name	[Text field]
Address 1	[Text field]
Address 2	[Text field]
Postcode	[Text field]
Country	[Dropdown menu]
Telephone	[Text field]
Telefax	[Text field]
E-mail	[Text field]



- Part 2.5.1.2 Batch control/testing:

Is it necessary to choose all possibilities as is stated in Manufacture License for company (if possible to find them there) or only for product, which we would like register?

Only the tests carried out for the products that the application is concerned should be listed here.

- Section 2.5.2:

There is empty field: what is necessary to write here? If I have different/multiple manufacturers responsible for any process I can use + and add it

The free text field is included so that a description of the partial product (e.g. vial with solvent, vial with powder, solvent etc. can be included if necessary to indicate which part of the product a specific manufacturer produces. This field is optional and can be left empty.

- Is it necessary to choose all possibilities as is stated in Manufacture License for company (if possible to find them there) or only for product, which we would like register?

Only the tests carried out for the products that the application is concerned should be listed here.

Section 2.6.1 Active substance/excipients :

It is not clear what is necessary to write to the first line.

Why is there also possibility to add this part if MAA should be prepared only for one product/strength?



2.6.1 Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s)

A note should be given as to which quantity the composition refers (e.g. 1 capsule)

Pharmaceutical Form 1 Capsule, soft

The composition and the strengths can only be defined in referencing a defined quantity, e.g. 1 (piece) capsule, hard or 100 ml solution.

• The same question relates to the screen below:

It is not clear what is necessary to write to strength.

Why is there also possibility to add this part if MAA should be prepared only for one product/stren



The strength of the product should be included in this field; for example 100 – the unit should be placed in unit field e.g. mg. The plus button can be used to repeat the line in case more than one strength is applied for, this can be used for example for CP applications.

Questions – Initial MAA form



• Section 2.6.1.:

There is possible to add API/excipients 2 times. Which is correct? Is it up to me?

The second question is relation the empty field above API or excipient:
There is possibility to write more information about API/ excipient – composition of flavours etc

2.6 QUALITATIVE AND QUANTITATIVE COMPOSITION
2.6.1 Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s)

A note should be given as to which quantity the composition refers (e.g. 1 capsule)

Pharmaceutical Form

(The values of the pharmaceutical form, strength and active substances fields have been populated from "Declaration" section.)

Strength Units

List the active substance(s) separately from the excipient(s)

Name of active substance	Quantity / Unit	Reference / Monograph Standard
ACETYSALICYLIC ACID		

Name of active substance	Quantity / Unit	Reference / Monograph Standard

Name of Excipient	Quantity / Unit	Reference / Monograph Standard
SEPIFILM 3048 YELLOW		

Name of Excipient	Quantity / Unit	Reference / Monograph Standard

This depends on the specific product and the application type. Specific details relating to the active substance and excipient can be added in the blue free text field which might be particularly useful for products containing more than one active substance or to specify parts of the product e.g. tablet core, film coating etc.



- If possible, I would need the confirmation that the eAF will be compulsory to use in MRP/DCP procedures from 1 January 2016 also for Vet procedure. In that case, how it will be handled by National Competent Authorities which are still requiring hard copies?

Yes, the use of the eAFs is also mandatory for Veterinary submissions as per the eSubmission Roadmap; Please contact the relevant NCA for national requirements.



- Pharmaceutical form: If our pharmaceutical form is not listed in the form, what should we do?

Please follow the defined missing term request process and send the request to mdms@ema.europa.eu. Further details are available on the eAF website.

- Active substance: When we click to the drop down window, there are no active substances to choose. Not even with writing the active substance and clicking the bottom “search”. The same happens with excipients

Occasionally there are issues with the connection to the EUTCT web services. If this happens, please save the form and reopen to check if the connection has returned. If the issue persists consult your IT support to check if your internet connection is working and there are no firewall settings preventing access to EMA webservice.

- In case the name of the product is not compliant with the current standard terms for pharmaceutical form (ie. “Solution for dental use” instead of “dental solution”), should a eAF Term Request Form be filled to add this pharmaceutical form to the drop-down list or should the EDQM standard term be selected in the drop-down list?

If a term is still missing in the Standard Term list, you should follow the eAF Term Request process. The agency will contact EDQM for a new term as appropriate and should inform you on the outcome of the process.



- Documents appended to this application: There are some boxes we don't need to mark as they are not applicable for us. However, if we don't mark all of them a validation error appears. What should we do?

Occasionally the built in business validation rules have been interpreted incorrectly when the forms were built. You should report any unusual form validation errors to eAF@ema.europa.eu. Please note that the form validation errors are there to guide you to fill in the application correctly and sometimes it is perfectly acceptable to leave some validation errors especially when information is provided on a separate annex to the application form.



- In terms of composition, how do I address situations when label claimed active substance is a base while the actual API used is a salt as per below example:

Material	Function	Quantity	Unit	Specification
Fluoxetine hydrochloride	Active substance	22.4	mg	E.P
Equivalent to Fluoxetine		20.0		

Currently the AF is completed as per below:

2.6.1 Qualitative and Quantitative composition in terms of the active substance(s) and the excipient(s):			
A note should be given as to which quantity the composition refers: 1 tablet			
List the active substance(s) separately from the excipient(s):			
Name of active substance(s)*	Quantity	Unit	Reference/Monograph standard
Fluoxetine	20.0	mg	
as			
Fluoxetine hydrochloride	22.4	mg	Eur.Ph

Detailed instructions how to add salt/hydrate format in section 2.1.2 of the Initial MAA for are available in the eAF Q&A document and in the technical guidance document.



• **Fast web view** / Our eCTD generating software automatically saves all pdfs within the eCTD with fast web view enabled, however in the case of signed eAFs this renders them unviewable, there is no way to switch this off. The workaround we have employed is to “print” the signed eAF to pdf which is then used in the eCTD. The “printed” pdf can have the fast web view enabled and remain readable even when output as part of an eCTD. My question is two fold Will this still be acceptable when the form becomes mandatory? When printing to PDF the bookmarks are lost, but we have been reintroducing them manually; if print to pdf is an option for eAF forms, is it necessary to reintroduce the bookmarks?

Printing and scanning to overcome the fast web view BP warning will destroy the XML-backbone (XML data) and results in an incompliant eAF which will be rejected. The eCTD validation best practise warnings can be ignored but the forms must be provided as real eAFs with xml. Flat PDFs will not be accepted. The validation criteria is being updated and in the new version the eAF will no longer be tested for fast web view.

• The eAF won't accept "Fast Web View" setting and so a warning is given when validating the NeeS.

The NeeS validation best practice warning can be ignored.



- Some users at our company are having issues populating the substance section of the eAF. Users based in France are able to populate the substance section, but users in North America are not. Users in North America receive warning messages. The issue occurs whether using Adobe Reader X or Adobe Standard X. It also occurs whether using version 1.18 or 1.19 of the variation form?
Drop-down lists and search fields within the forms are populated dynamically from eAF's web services (managed by the EMA).

Additional, dynamic information is 'called' by the form as soon as it's opened and trusted. This then populates certain drop-down option lists and searches with data from EMA's web services

- If your local IT policy forbids you from making changes to a security setting, it is recommended that you contact your local IT service desk and request that they allow access to the following url:
<http://eaf.ema.europa.eu/eaf/services/EutctService?wsdl>

IMPORTANT: This web services location, managed by the EMA, enables many of the forms' fields, searches and drop-down lists to be populated dynamically. Without access, the form CANNOT be completed.

- To check in Acrobat 10 and above, select Edit>Preferences then choose the Security (Enhanced) category. If you are able to, add the full path of the file in the 'Privileged Locations' table. If you are not, contact your IT service desk and request that access for the form(s) to the EMA's web services (using the above URL) is allowed.



- **eAF for initial MA application** / Section 1.3 for the legal basis cannot be completed (the boxes which should normally be ticked (e.g. 1.3.1 for Art. 12(3)) do not pop up);

Please provide more details of this issue ideally with screenshots comparing it to the NTA application form.

- For the GMP-related information (5.9 and 5.10), there is a technical mismatch between the information ticked in the eAF and the automatic ticked boxes in the Annex to the eAF.

We are unable to reproduce this issue. Could you please provide us a copy of the form where this issue is present for further investigation.

- The section “Active Substance” is difficult to fill in especially for immunological products.

The AS descriptions available in the database most often do not match very well with the description in the product information. Clear instructions on the level of detail that is required should be given. Is a workaround available to indicate the immunological active substances in more detail?

The same workaround principle applies as for other sections, please attach an annex to the application form. Please highlight a respective use of annex in your cover letter.



- Why is there no possibility any more to add a contact person for the Scientific Service for the CP? The User guide states the following: “In centralised procedure a single contact person should be indicated for the scientific service”.

For ease of contacting the applicant only single contact person for each procedure should be provided. Contact details can contain an email address to a shared mailbox if multiple persons are dealing with the application on the applicant side.

- In section 2. Product name/strength/form is not listed in the form as there is a reference to Annex A.

MA Holder name: reference to Annex A is given as option, however Annex A does not list MAH in Annex A for a CP.

As for CP there is only ever one MAH, this field can be filled in the eAF and the rest of the information is provided in the Annex.



•Regarding section 2.5.2 and 2.5.3: does the term “quality control” also includes release testing, and if so, when it comes to the release testing of the medicinal product, are then sites listed twice, once in 2.5.1.2 and 2.5.2?

Yes, release testing of the finished product is part of Quality testing. This activity is only linked to sites performing Batch Control testing arrangements in relation to the Batch Release of the product as per requirements of Article 51 of Directive 2001/83/EC. As such a site may perform both release testing under 2.5.1.2 and “normal” QC-FP activities under 2.5.2 which are not linked to the batch release. In this case the site(s) will be listed twice i.e. under each section. However, if the site only performs one or the other quality control testing only, the site(s) will then need to be listed in the relevant section depending on the QC-FP activity. testing arrangements in relation to the Batch Release of the product.

Sometimes, sites perform both kinds of testing activities however only sites located in the EEA or where an MRA or ACAA arrangement is in place can be listed in 2.5.1.2. Third country sites (USA and any other country outside the EEA/MRA/ACAA) cannot perform this activity and should therefore not be listed under 2.5.1.2. These sites are only authorised to perform QC-FP activities not related to the Batch Release.



- Could you probably address how notifications, e.g. art 61(3) will be handled in the future?

The eAF does not introduce change to how art. 61(3) notifications are handled.

The existing paper form as published on the CMDh website has not been replaced and should be used as previously. There are no plans to replace this MS word template in near future.

MAA Application form:

- Section 2.2.1: The “OK/Clear/Cancel” button doesn’t work?

Section 2.2.1 is auto-populated from the declaration section.

- Section 2.5.3: The field “Name of the manufacturer if different from the above” is mandatory – but “Name of the CEP holder” isn’t – why is that, and how can a field containing “if” be mandatory?

More information and details required to allow investigation.



- For product with more than one API: How do you list the strength of the product in the applications forms? As it is now you will have to list the amount of the individual APIs in separate rows with no link to the API?

Example of how the form could be filled below

Product (invented) name Wonderdrug 100mg/10mg

Pharmaceutical Form: Capsule, hard

Strength:	Units
100	mg

Active Substance(s):
PARACETAMOL

Add Active Substance(s)

Pharmaceutical Form:

Strength:	Units
10mg	mg

Active Substance(s):
CODEINE



•According to the current requirements section 3.2.P.1 and section 2.6.1 of the AF need to be harmonised and the naming of the substances has to be in accordance with the European Pharmacopeia naming, when applicable. Why controlled vocabularies in respect of active substances & excipients used for drop-down lists of section 2.6.1 are not harmonised with the European Pharmacopeia naming?

EP	eAF
Cellulose, microcrystalline	Microcrystalline cellulose
Hypromellose	Methyl hydroxypropyl cellulose

Answer to be provided in writing following investigation.

•Why controlled vocabularies in respect of excipients are not harmonised with the controlled vocabularies used for xevmpd since the MAHs have to comply with both when uploading the data/completing the section 2.6.1?

For example we have been requested that for hypromellose, it is necessary to state both the substitution type & the nominal viscosity, but for hypromellose 2910/E5 there is no harmonisation. The only common name available in both xevmpd & eAF is "Hypromellose E-5", but this one does not indicate the substitution type?

Answer to be provided in writing following investigation.



- In the case of a very urgent submission (the same day that the problem is encountered) and the eAF cannot be opened, nothing is not working properly, I cannot sign the document, etc... How long is the response time for the eAF team to come back to me and solve the problem?

Please contact eAF@ema.europa.eu immediately highlighting the urgency of the query in the message.

- Would there be the possibility for very exceptional cases to submit the latest AF version 2015 and put a comment in CESP? What would be your proposed solution for such a situation?

Please be aware that the RMS may ask for a compliant version during validation. The EMA will reject all non eAFs.



• **Publishing requirement of eAF** / Is there a requirement for the eAF to be supplied in a published submission only (i.e. eCTD /NeeS)? Or can the eAF be submitted via CD as a standalone document too?

Please submit the eAF always within a eCTD / NeeS / VNeS submission. However, if your dossier format is still paper based, a separate electronic submission may be appropriate if agreed with the responsible NCA.



- We usually publish our regulatory dossiers in NeeS format. Do we have to incorporate the eAF into the NeeS (in module 1.2) or do we have to submit the eAF separately from the?

Please submit the eAF always **within** the NeeS submission. You should not submit a separate eAF outside the NeeS dossier.

- If the eAF has to be submitted separately from the NeeS, where should it be submitted?

Please always submit eAF within the NeeS submission.



- In the eAF there are fields for local representative information, but no provision for a field to enter a title such as “Variation coordinator during the procedure”. Could such a field be in the form in the future?

The eAFs reflect the NTA requirements. If the ‘variation coordinator’ details are required by the receiving bodies, an NTA change request can be submitted.



Contact

Please send any questions to

eaf@ema.europa.eu or the responsible NCA contact