



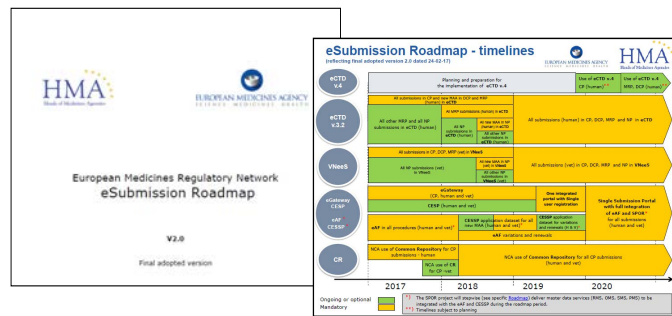
WORKSHOP 3: How to successfully prepare electronic submissions for CEPs

EU eSubmission Roadmap

Karin Gröndahl, Swedish MPA



eSubmission Roadmap



- HMA eSubmission Roadmap**
- Final HMA eSubmission Roadmap (adopted) The final updated version of the eSubmission Roadmap 2.0 was adopted by the EU TMB on and endorsed by the HMA on the 24th of February 2017. Roadmap will be published to reflect further details on the practical implementation steps.
 - eSubmission Roadmap (visual representation) The final updated version of the eSubmission Roadmap v2.0 visual representation of the timelines.
- Annexes to the eSubmission Roadmap**
- Annex 2 to the HMA eSubmission Roadmap on the implementation of mandatory use of eCTD format for regulatory submissions. This revised version of the annex 2 to the roadmap has been adopted.
 - Annex VI to the HMA eSubmission Roadmap on the implementation of mandatory use of VNeS format for Veterinary regulatory submissions. This revised version of the annex VI to the roadmap has been adopted.



eSubmission website – CMB Documents

eSubmission
CMB Documentation

Human eSubmission
 - **Human eSubmission**: These documents have been created/adopted by the eSubmission CMB or by the TIGEs.
 - **Human eSubmission Roadmap**:
 - Final HMA eSubmission Roadmap (adopted): The final updated version of the eSubmission Roadmap 2.0 was adopted by the EU TMB on and endorsed by the HMA on the 24th of February 2017. The summary of main changes is available in the [Release Notes](#). Updated Annexes to the Roadmap will be published to reflect further details on the practical implementation steps.
 - eSubmission Roadmap (visual representation): The final updated version of the eSubmission Roadmap v2.0 visual representation of the timeline.
 - **Annexes to the eSubmission Roadmap**:
 - Annex 2 to the HMA eSubmission Roadmap on the implementation of mandatory use of eCTD format for regulatory submissions. This revised version of the annex 2 to the roadmap has been adopted by the eSubmission CMB on 10th March 2017.
 - Annex VI to the HMA eSubmission Roadmap on the implementation of mandatory use of VNeES format for Veterinary regulatory submissions. This revised version of the annex VI to the roadmap has been adopted by the eSubmission CMB on 06 May 2017.
 - [VNeES Annex Questionnaire example](#)

Veterinary eSubmission
 - **Veterinary eSubmission**: These documents have been created/adopted by the eSubmission CMB or by the TIGEs.
 - **Veterinary eSubmission Roadmap**:
 - Final HMA eSubmission Roadmap (adopted): The final updated version of the eSubmission Roadmap 2.0 was adopted by the EU TMB on and endorsed by the HMA on the 24th of February 2017. The summary of main changes is available in the [Release Notes](#). Updated Annexes to the Roadmap will be published to reflect further details on the practical implementation steps.
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Documents
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 - [VNeES Annex Questionnaire example](#)

Guidance
 - **TIGEs/CMB Harmonised eCTD Guidance**:
 - The EU Harmonised technical eCTD guidance version 4.0
 - The SPG for the use of eCTD in MRP/DCP version 4.0
 - eCTD validation criteria v5.1 with Release notes - 12/2016: The use of validation criteria v5.1 is mandatory as of 1st October 2016.
 - Variations in eCTD format: GSA document covering practical issues for variations in eCTD format
 - Validation criteria GSA 05/04/2017 [New](#)

Guidance
 - **TIGEs/CMB Harmonised VNeES Guidance**:
 - The TIGEs Harmonised VNeES guidance document version 4.0 can be found [here](#) and Release notes [here](#) (Note: The guidance is not applicable to centralised procedure)
 - VNeES Validation Criteria v4.1 and Release notes - The use of validation criteria v4.1 is mandatory as of 1st October 2016.

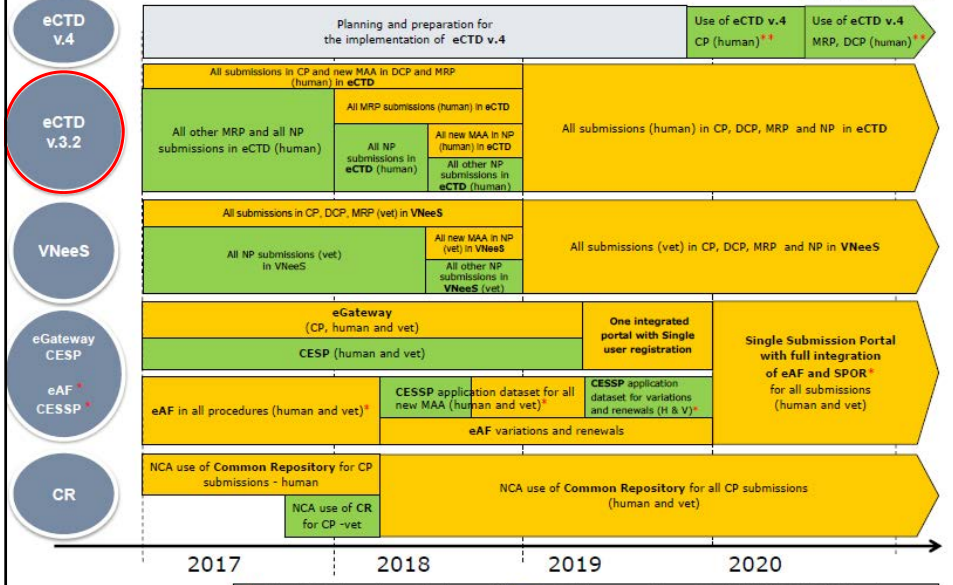
Guidance
 - **EMA eSubmission Guidance for the Centralised Procedure**:
 - All EMA guidance documents, both practical and strategic, as well as Statements of Intent relating to eCTD and electronic submissions, can be found on the EMA external website [here](#).

Best Archiving Practice
 - [Best Archiving Practice Guidance](#)
 - [Best Archiving Practice Specification](#)

EUROPEAN MEDICINES AGENCY

eSubmission Roadmap - timelines

(reflecting final adopted version 2.0 dated 24-02-17)



Ongoing or optional (Green) Mandatory (Yellow)

* The SPOR project will stepwise (see specific [Roadmap](#)) deliver master data services (RMS, OMS, SMS, PMS) to be integrated with the eAF and CESSP during the roadmap period.
 ** Timelines subject to planning

Annex II to the eSubmission Roadmap

10 March 2017

Annex 2 to the HMA eSubmission Roadmap: Implementation of mandatory use of eCTD format for regulatory submissions

Status: Final updated version adopted by the eSubmission CMB

Scope

This annex is intended for both applicants and national authorities and describes details:

- to be monitored during implementation;
- for additional guidance to support a smooth processing of eCTD submissions and to avoid uncertainties on how to handle eCTD correctly;
- on aspects to be mitigated to cover concerns and identified hurdles.

Stream II, which refers to the implementation of eCTD as per the HMA eSubmission Roadmap, only applies for products for human use, since veterinary products are handled in another stream. The outline of stream II defines different steps for implementation:

Mandatory eCTD in European Procedures

Use of eCTD for all regulatory activities in European procedures (DCP/MRP) by 1 January 2018

- This refers to all submission types for a dossier such as variations, renewals, PSURs, ASMFs and so on.
- No baseline submissions are required, however, it is recommended to consider a submission of baseline for module 3 in which case the relevant guidance should be followed.

Mandatory eCTD in National Procedures

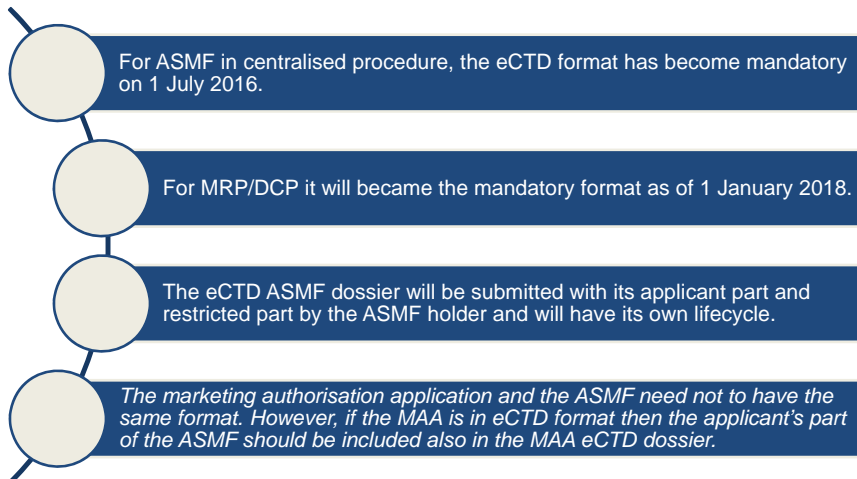
Use of eCTD for new MAA in NP by 1 July 2018

- This step has been added to the updated version of the eSubmission Roadmap to strive for a harmonised approach within the EU....

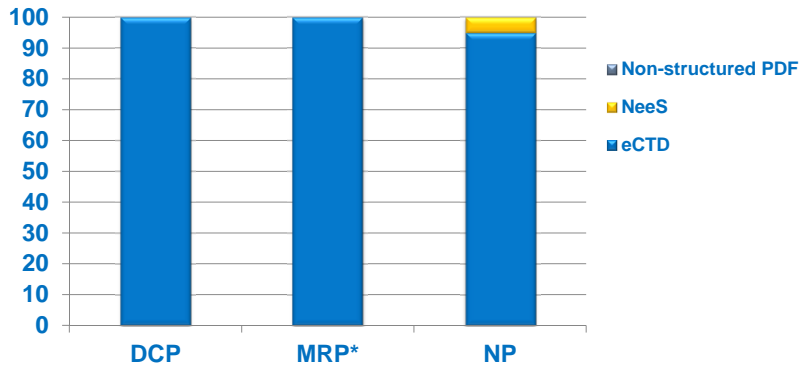
Use eCTD for all regulatory activities in National Procedures (NP) by 1 January 2019

- This step refers to all submission types for a dossier such as variations, renewals, PSURs, ASMFs and so on..... No baseline submissions are required, however, it is recommended to consider a submission of baseline for module 3 in which case the relevant guidance⁶ should be followed.

From Annex II to the eSubmission Roadmap



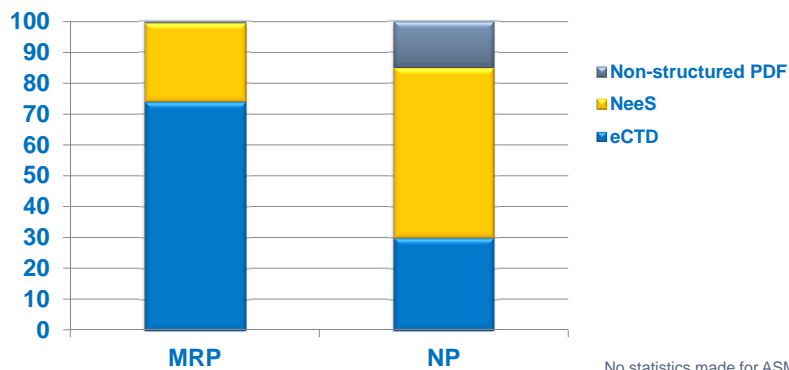
Statistics: New MAA submitted to the MPA Q1-2 2017 Format (% of total submissions)



Submissions in total: 119 in DCP, 22 in MRP and 21 in NP

*) MRP: Format by the start of the MR procedure

Statistics: Variations submitted to the MPA Q1-2 2017 Format (% of total submissions)



Submissions in total: 2330 in MRP and 662 in NP

No statistics made for ASMF, but estimation is about 100% for WS-ASMF, about 50% for other ASMF in MRP/DCP and about 10% in NP

EU Region eCTD Validation Criteria

Version 6.1

March 2016

eCTD Validation criteria

Document Change Control eCTD Validation Criteria File-Folder Structure & Names Files and Folders Q&A Picklist Values

Number	Category	Validation Criterion	Type of check	Lifecycle needed? 'YES'	Comments
1.1	ICH DTD	The specified filename is used	RF		File is named 00-e00-5-2.doc
1.2	ICH DTD	The file is placed in the correct folder	RF		In the folder /XXXXXX/0000000000
1.3	ICH DTD	A currently acceptable version of the DTD is used (checksum matches the published value)	RF		Currently acceptable versions are described in the current ICH eCTD Specification. The checksum for the DTD in eCTD v3.2 (ich-ectd-3-2.doc) is 1.68f931c0d86357f544e378e5f79a27f
1.4	ICH DTD	The version number of the DTD/application used in the sequence being tested is higher than or equal to the version of the DTD used in the sequence numerically preceding the incoming sequence in the eCTD lifecycle	RF	Y	With reference to any transition guidance, going back to an earlier version is not allowed when a newer version has already been used for that eCTD. The sequence numerically preceding the incoming sequence in the eCTD lifecycle refers to the highest numbered sequence that is numerically lower than the incoming sequence. The criterion should only be tested if there are sequences with lower sequence numbers present.
1.5	ICH DTD	The version number of the DTD/application used in the sequence being tested is higher than or equal to the version of the DTD used in the sequence numerically succeeding the incoming sequence in the eCTD lifecycle	RF	Y	The rule specifically tests in situations where sequences have been submitted out of order. The sequence numerically preceding the incoming sequence in the eCTD lifecycle refers to the lowest numbered sequence that is numerically higher than the incoming sequence. The criterion should only be tested if there are sequences with higher sequence numbers present.
2.1	ICH sky/sheet	The specified filename is used	RF		File is named e000-2-2.xls
2.2	ICH sky/sheet	The file is placed in the correct folder	RF		In the folder /XXXXXX/sky
2.3	ICH sky/sheet	The checksum for the sky/sheet used must match the published checksum for the spreadsheet associated with the DTD used for the sequence	RF		For example, the checksum corresponding to the sky/sheet from eCTD specification v.2 (ectd-2-2.xls) is 3a7fa202455e95f4a2e02035b6449377
3.1	EU M1 DTD	The specified filename is used	RF		File is named eu-regional.doc
3.2	EU M1 DTD	The file is placed in the correct folder	RF		In the folder /XXXXXX/0000000000

m3
m3-boc.pdf
32-body-data
32e-drug-sub
drug-substance multiple branches possible
32s1-gen-info
structure-var.pdf
general-properties-var.pdf
32s2-manuf
manufacturer-var.pdf
manuf-process-and-controls-var.pdf
control-of-materials-var.pdf
control-critical-steps-var.pdf
process-validation-var.pdf
manuf-process-development-var.pdf
32s3-charac
elucidation-of-structure-var.pdf
impurities-var.pdf
32s4-contr-drug-sub
control-var.pdf
32s41-spec
specification-var.pdf
32s42-analyt-proc
analytical-procedure.pdf
32s43-val-analyt-proc
validation-analy-procedure.pdf
32s44-batch-analyt
batch-analysis-var.pdf
32s45-justif-spec
justification-of-specification-var.pdf
32s5-ref-stand
reference-standards-var.pdf
32s6-cont-closure-sys
container-closure-system-var.pdf
32s7-stab
stability-summary-var.pdf
postapproval-stability-var.pdf
stability-data-var.pdf



Important eCTD related documents

- eCTD Specification ([v 3.2](#))
- EU eCTD Module 1 Specification ([v 3.0.2](#), April 2017)
- Harmonised Technical Guidance for eCTD Submissions in the EU ([V 4.0](#), April 2016)
- eCTD Validation criteria ([V 6.1](#), July 2016)
- *Draft* Practical Guidance on the use of the eCTD format for ASMF for Active Substance Master File Holders and Marketing Authorisation Holders MAHs ([draft v 1.5](#))





Thank you for your attention