17 December 2021

Release notes for version 5.0 of the Harmonised Technical Guidance for eCTD Submissions in the EU

This new version has been drafted by the Human Harmonisation Group and reviewed by the eSubmission Expert Group and the CMDh before it was adopted by the eSubmission Expert Group in December 2021.

Since it was very long since the guidance was updated, it has been an extensive review of the document and there are changes made in almost all sections. Mainly, the updates are made to improve the wordings and clarify some issues where questions from applicants have been raised over time. Furthermore, some text is now included in this guidance that was earlier published as Q&As.

The update also reflects the mandatory use of eCTD and submissions through portals as well as mandatory use of tracking tables in all procedures as stated in the latest update of the EU M1 eCTD specification.

In some sections, applicants should pay extra attention to the updates (see below) and therefore some text is also copied to this document.

2.9.11 Technical Validation of eCTD Submissions

Note specifically the new text as copied below.

"Errors found during the content validation e.g. mistakes in an application form to be corrected, should be resolved through the submission of a new eCTD sequence using the next sequence number. These errors, which are content errors, must never be resolved by resubmitting an existing sequence by re-using the same sequence number.

An exception to this would be if the envelope is incorrect and it is requested by an agency to be corrected and resubmitted with the same sequence number. In such scenarios, the updated sequence (same sequence number) should only be submitted to the requesting agency."

2.10.3 Signatures

Note specifically the new text as copied below.

"Electronic signatures are regulated in EU by Regulation (EU) No 910/2014 of the European Parliament and of the council of 23 July 2014 on electronic identification and trust services for electronic transactions in the internal market and repealing Directive 1999/93/EC. For applications of Marketing Authorisations including post-authorisation submissions, most NCAs and EMA do not require wet or digitally signed cover letters or application forms if submitted through a portal (e.g. CESP and EMA Gateway) with logon credentials. However, some NCAs still require additional signatures and might accept wet signatures, scanned signatures and/or electronic signatures as specified in the CMDh document 'Requirements on submissions for New Applications within MRP, DCP or National procedures' and 'Requirements on submissions for Variations and Renewals within MRP and National procedures'.

For EMA submissions, in general qualified and advanced electronic signatures as per the European Commission eIDAS regulation (Regulation (EU) No 910/2014) are accepted."

2.11.3 Re-Baselining a Broken eCTD Lifecycle

Note specifically the new text as copied below.

"However, when compiling (merging) several eCTDs built per strength and/or dosage form of a product into only one combined eCTD for that product, normally one of the existing eCTD lifecycles would be kept and be completed with the missing documents from the current view of the other strengths and/or dosage form eCTDs to give the complete current dossier. In those cases, the assigned UUID of the maintained eCTD (the chosen strength or dosage form built upon) will also serve as UUID for the future (merged) lifecycle. The strategy for merging of eCTDs should be agreed with the relevant authorities in advance."

2.12.1 Portals/Gateways

Note updated text on CESP and EMA eSubmission Gateway and National portals.

2.12.2 CD / DVD

Note reduced text on CD/DVD submissions, since this is very seldom used nowadays.

3.2.3.2 Tracking Table

Note specifically the new text as copied below.

"A tracking table should always be included as an annex to the cover letter for submissions within all procedures. The file should be named cc-tracking-var.pdf and be placed in /XXXX/m1/eu/10-cover/cc (e.g. ema-tracking-var.pdf for a CP, common-tracking-var.pdf in an MRP/DCP, or be-tracking-var.pdf in a NP.)

Examples of Tracking tables to be used within the MRP/DCP are found in the CMDh guidance 'CMDh Best Practice Guide on the use of eCTD in the MRP/DCP' An example of a Tracking table that would be suitable for a centralised or a national procedure can be found in Annex 2."

3.4 Module 3 Quality Folder

This section has been extensively updated to give better guidance on how to structure documents within module 3. Many eCTD dossiers are currently not very well structured in Module 32s and Module 32p and this updated guidance should now help improving this to facilitate assessment.

Please note: "*If an existing eCTD is not structured in line with the given guidance, the dossier should be restructured with the next submission of a quality variation that affects the relevant content."*

4.2 Variation Applications

Note specifically the new text as copied below.

"The submission type should reflect the type of variation. (See Q&A for Variations in eCTD). Submissions for workshare/grouping variations (containing MRP/DCP/National products only) concerning several eCTD submissions are recommended to be supplied together in a single zip file, refer to section 2.12. The zip file should contain clearly marked subfolders for each product eCTD dossier (each specific UUID) that takes part in a worksharing or grouping procedure.

For worksharing procedures containing only CAPs or worksharing procedures containing CAPs and MRP/NAPs a separate submission for each eCTD via the eSubmission Gateway/Web Client only is required. In case of worksharing procedures containing CAPs, the submissions for nationally authorised products (MRP/DCP/NP) should be sent to EMA only via the eSubmission Gateway/Web Client. There should be no additional submissions directly to NCAs."

4.5 PSURs

Note, this section has been extensively updated to be in line with information already published e.g. in Q&As or on the eSubmission website.

4.6.2 EMA-led referral procedures

Note specifically the new text as copied below.

"Referral submissions concerning CAPs only and all EMA-led referrals where also National products are included (NP, MRP, DCP products) should be sent via EMA eSubmission Gateway or eSubmission Web Client only. They are available via the Common Repository and considered delivered to all National Competent Authorities (NCAs) and scientific group experts. No additional copies of the submissions should be sent directly to the NCAs as this might lead to validation issues and cause delays.

For CAPs, referral submissions should always be submitted as the next sequence in the product lifecycle for each CAP. Standalone eCTD submissions for the referral (on active substance basis) are not allowed for any CAPs included in referral procedures. However, for EMA led referral procedures where only MRP, DCP and NP products are included, a stand-alone eCTD lifecycle is recommended to cover all the concerned nationally authorised products."

4.7 Active Substance Master Files

Note specifically the new text as copied below.

"For Marketing Authorisation Applications (MAAs) in eCTD format, where the documentation on the active substance is presented as an Active Substance Master file (ASMF), the applicant should incorporate the applicant's part (AP) documents of the ASMF and the Quality Overall Summary (QOS) on the applicant's part of the ASMF into the eCTD structure as per the relevant guidelines. It is recommended to use a suffix of '-ap' on the filename of these documents.

The ASMF Holder should provide the full ASMF, i.e. both the Applicant's and the Restricted part in eCTD format to the relevant authorities. The Applicant's part and the Restricted part should each have a front page clearly stating the version number and date.

The ASMF should include a QOS on the Applicant's part and a separate QOS on the Restricted part. Each QOS should have a front page clearly stating the version number and date."

Annex 2, Former **Guidance on Text Searchable Documents**

The content in Annex 2 has been changed from *Guidance on Text Searchable Documents* to **Tracking Table Example** and include an example of a tracking table to be provided with applications within national or centralised procedures.

Annex 3, Guidance and Best Practice on the Structure of Module 3

A lot of examples have been deleted since they were outdated or not in line with the new updated text in section 3.4 (see above). **A3-3.2.1** now includes new examples.