Release Notes for
Harmonised Technical Guidance
for eCTD Submissions in the EU v3.0

This document highlights the changes incorporated in version 3.0, in comparison with version 2.0, of the eCTD guidance document. For clearer guidance, it is recommended that the full version of the updated document be read.

Section	Previous Section No. in v2.0	Changes
General Changes throughout the document	NA	References to TIGes (Telematics Implementation Group – Electronic Submissions) have been removed
Cover Page	NA	Changed the title of the Document, version number, and date.
1. Introduction	1.	Included information on Q&As published in between versions of this guidance
2.1.2 Types of Submissions	2.1.2	Added withdrawals to submission types enumerated
2.1.3 Types of Procedures	2.1.3	Added reference to guidance to be used for MRP and DCP submissions
2.1.4 Exceptions	2.1.4	Added a general statement at the end of the section that this guidance does not apply to dossier content explicitly excluded from the commonly maintained electronic dossier. Reference to the CMDh Best Practice Guide for further exceptions was also added.
2.4 Moving to eCTD Format from Paper or NeeS Type Applications	2.4	Throughout the section, minor editorial changes were done to improve readability. In the 1st paragraph, added a rationale for the recommendation for a baseline submission. In the 2nd paragraph, deleted some detail which are covered in Section 2.12 In 3rd paragraph changed reference to CMDh Best Practice Guide for eCTD in MRP and DCP into reference to CMDh guidance 'Requirements on submissions (eCTD and NeeS) for New Applications within MRP, DCP or National procedures'
2.5.2 File Naming	2.5.2	Removed version number of eCTD validation criteria, and used 'current' instead.
2.5.3 Placement of Documents	2.5.3	Added an example of an exception to leaf placement at the lowest level of the CTD structure.

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2.6 Correspondence	2.6	Minor editorial changes to improve readability
2.7 Paper Requirements	2.7	Rewritten so this only references to the CMDh guidance on submission requirements
2.8 Hardware	2.8	'zip drive' was changed to 'external hard drives'
2.9.1 File Formats	2.9.1	In 1st paragraph added EMA as requestor of files in MS Word Deleted 2nd paragraph on the use of XML for application forms
2.9.2 Portable Document Format (PDF)	2.9.2	Added the document title for the ISO Standard for PDFs Added PDF versions 1.5, and 1.6 as versions normally to be used Deleted 4th bullet point in previous version, which mentioned how to handle when it is unavoidable to use other PDF versions Differentiated key requirements and requirements to consider Added the requirement that fonts used in PDF should be embedded where possible and that rendition to PDF should preferably create documents which are "tagged" Added reference to ICH M2 recommendations at the end of the section.
2.9.3 Sequence Numbers	2.9.3	Changed information on the Tracking Table Added rationale for submitting sequences in numerical order Deleted reference to CMDh recommendations on the cover letter
2.9.4 Related Sequence	2.9.4	Revised the first sentence to read "The relationship of one sequence to another is managed using the related sequence attribute in the envelope in eu-regional.xml" In 2nd paragraph added an example (Variation application) for a Regulatory Activity
2.9.5 Leaf Lifecycle Operation Attributes	2.9.5	Changed heading to 'Leaf Lifecycle Operation Attributes' Rewritten to implement CR 20121004/Q&A40.

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2.9.7 Node Extensions	2.9.7	Corrected to reflect that node-extensions are useful to group together multiple leaves, not files. Indicated that currently there is no provision for additional folders in m1-responses, therefore the use of an additional folder in combination with a node-extension is not allowed.
2.9.9 Other File Formats	2.9.9	Added numbering and title to figure
2.9.10 Technical Validations of eCTD Submissions	2.9.10	Minor editorial changes to improve readability
2.10.4 Signatures	2.10.4	Removed 'Electronic' from section title Minor editorial changes to improve readability Added reference to CMDh guidance for requirements on wet or scanned signatures Added references to EMA websites regarding electronic submissions
-	2.10.5	Removed section 'Transmission Media' as the information is already covered by other sections
2.10.5 Procedure for Sending Electronic Information	2.10.6	Completely rewritten to improve readability Removed detail on size limit for EudraLink Included CESP and eSubmission Gateway information Included information on current standard for burning CDs/DVDs Moved recommendation to supply multiple eCTD submissions for workshare/grouping variations on a single CD/DVD to section 4.2
2.10.6 Labelling/Metadata	2.10.7	Changed heading from 'Labelling of Media' to 'Labelling/Metadata' Minor editorial changes to improve readability Changed "full application number(s) (if known)" to "full procedure number(s) (if known) (e.g. UK/H/1234/001-005/II/0034)"
2.11 Number of Media Requested	2.11	Moved information on current standard for burning CDs/DVDs to section 2.10.5
2.12 Technical Baseline Applications	2.12	Reworded 3rd paragraph and included instruction to use submission type *reformat* for the baseline sequence

Section	Previous Section No. in v2.0	Changes
2.12.2 Baselines Starting Later in Lifecyle	2.12.2	In 3rd paragraph added title of CMDh guidance Removed last paragraph containing information on consequence for life cycle management
2.12.3 Re-Baselining a Broken eCTD Lifecycle	2.12.3	Changed '..prior written agreement of the receiving agency..' to '.. prior agreement between the MA holder and the receiving NCA..' Added 3rd scenario and examples
3.1 General Information	3.1	Removed last paragraph on inability to make cross references across eCTD applications (already covered in 2.9.7)
3.2.2 Creation and Management of Envelope Information	3.2.2	Removed allowance to use 'to be advised' for Number. In case of worksharing submissions and for submissions of grouped Type IA variations that affect multiple marketing authorisations a high-level submission number must be provided in all cases. Removed duplicate information on 'Submission Type'
3.2.3.1 Cover Letter	3.2.3.1	Added requirement that content of cover letter submitted in paper must me identical to the one submitted in eCTD Added instruction that a clarification note may be provided when resubmitting content due to technical validation or sequences missing at NCA side and that the original cover letter in the eCTD should not be changed
3.2.3.2 Tracking Table	3.2.3.2	Changed 'CC-cover-tracking.pdf' to 'CC-tracking.pdf' Removed 'CC-cover-tracking.xml' Updated examples accordingly (incl. emea to ema)
3.2.4 Application Forms	3.2.4	In 3rd paragraph changed 'Most NCAs do require' to 'Some NCAs do require' Included information on the use of the electronic application form

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3.2.5 Product Information	3.2.5	In 2nd paragraph added the need to provide the tracked changes in PDF for product labelling or risk management plan documentation in the Centralised Procedure In 3rd paragraph removed additional information on how to handle national translations for Type IA or IB variations and changed reference to CMDh BPG for eCTD in MRP/DCP into reference to CMDh guidance 'Requirements on submissions (eCTD and NeeS) for New Applications within MRP, DCP or National procedures' Reworded 4th paragraph to improve readability
3.2.6 Use of Response Documents Section	3.2.6	Indicated operation attribute 'append' should be avoided (in 1st paragraph) Added recommended format for filenames and included examples (conform Q&A36)
3.2.7 Use of Additional Data Section	3.2.7	Added the use for justifications for active substances or justification of eligibility of the product of the Centralised Procedure as an exemption for the Additional Data section
3.3.2 Structure of Module 2 Documents	3.3.2	Rewritten to improve readability Removed recommendation to use additional descriptive text in the leaf title Removed instruction to justify the absence of data in module 3-5 in the summaries instead of submitting place holder files Included reference to 'File-Folder Structure & Names' tab in the EU Validation Criteria spreadsheet

Section	Previous Section No. in v2.0	Changes
4.1 Initial MA Applications	4.1	Table 6: Added bulletpoint 'Final mock-ups reviewed during the procedure' in last Day Number/Milestone Table 7: Indicated in heading that the table is for Centralised Procedure Changed reference to CMDh Best Practice Guide on the use of eCTD in MRP/DCP into reference to CMDh guidance 'Requirements on submissions (eCTD and NeeS) for New Applications within MRP, DCP or National procedures'
4.2 Variation Application	4.2	Included recommendation to supply multiple eCTD submissions for workshare/grouping variations on a single CD/DVD Replaced information on parallel variations by a reference to Annex 4 Included a note that *technically* invalid Type IA variations should be corrected and resubmitted as required for any other eCTD sequence Table 9: Indicated in heading that the table is for Centralised Procedure Changed milestone 'Opinion + 75' to 'Opinion + 30' and noted this applies for Type II variations which are not followed by an immediate Commission Decision Added milestone 'Commission Decision + 5' for Type II variations following worksharing or with immediate Commission Decision Table 10: Indicated in heading that the table is for Centralised Procedure Added day number 'RSI Submission deadlines' Table 11: Indicated in heading that the table is for Centralised Procedure

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		Added reference to CMDh guidance 'Requirements on submissions (eCTD and NeeS) for New Applications within MRP, DCP or National procedures'
4.4 Renewal Submissions	4.4	Table 12: Indicated in heading that the table is for Centralised Procedure Table 13: Indicated in heading that the table is for Centralised Procedure Added reference to CMDh guidance 'Requirements on submissions (eCTD and NeeS) for New Applications within MRP, DCP or National procedures'
4.5 PSURs	4.5	Included information on how to handle single assessment PSURs
-	4.6	Removed section 'MRP and DCP Applications'
4.6 Referrals	4.8	Only numbering changed
4.6.1 Referrals handled through CMDh	4.7.1	Only numbering changed
4.6.2 Referrals handled through the centralised procedure	4.7.2	Only numbering changed
4.7 Active Substance Master Files	4.8	Numbering changed Removed option to provide ASMF as a stand-alone eCTD Added instruction to incorporate applicant's part (AP) into the eCTD structure and to use a suffix in the filename (-ap) Included reference to guidance document for ASMF in eCTD format
4.8 Vaccine Antigen Master Files	4.9	Only numbering changed

Section	Previous Section No. in v2.0	Changes
4.9 Plasma Master Files	4.10	Numbering changed Changed 'The complete PMF can be processed with its own submission/case/procedure number separately' into 'The PMF will be handled as a standalone dossier'
4.10 Applicant Initiated Withdrawals	4.11	Minor editorial changes to improve readability Moved information on applicant withdrawal for a variation, or parts of a grouped variation, during assessment to new section 4.13
4.11 Applicant Withdrawal or Agency Rejections of Regulatory Activities	-	Newly added section on how to handle fully or partially withdrawn or rejected regulatory activities
Annex 1: eCTD Reference Documents	Annex 1	Updates references to include current links Included reference to EU Module 1 Specification Provided links to EMA Q&As for Pre-submission guidance and Post-authorisation guidance separately Included references for EMA Gateway, CESP and eAF websites
A3-1.1 Attribute Infromation in the eCTD XML	A3-1.1	Changed "Electronic" to "Attribute" in the heading Minor editorial changes to reflect this paragraph concerns the XML attributes
A3-3.4 Excipients	A3-3.4	Removed sections on Compendial Excipients (A3-3.4.1) and Non-Compendial Excipients (A3-3.4.2) and replaced this by a reference to ICH eCTD IWG Q&A#73
A3-3.4.1 Excipients of Human or Animal Origin and Novel Excipients	A3-3.4.3	Only numbering changed