Release Notes for TIGes eCTD Guidance – Comparison of version 2.0 with 1.0

Section	Previous section number (version 1.0)	Changes
General Changes throughout the document	NA	EMEA changed to EMA
Cover Page	NA	Draft status of document removed. Changed the name of the document.
1. Introduction	1	Fully rewritten to align with Introduction of NeeS Guidance 2.0.
1.1 Glossary	1.1	Modified description of 'eCTD application' to remove referenece to Global Marketing Authorisation.
2.1.1 Types of Product	2.1.1	Included the word EEA to clarify the scope.
2.1.2 Types of Submission	2.1.2	Included ASMF and PMF as types and provided reference to guidance documents for variations.
2.1.4 Exceptions	2.1.4	Included Orphan drug designations and PIP submissions as exceptions.
2.2 Structure of Submissions	2.2	Minor change: removed 'with any one invented name' from the description of an eCTD application.
2.4 Moving to eCTD format from paper or NeeS type applications	2.4	Fully rewritten to provide more detailed information on when and how to move from paper or NeeS to eCTD and the consequences for further submissions and other ongoing regulatory activities. Included explanation on baseline submissions when moving from NeeS to eCTD. Included description on handling historical sequences in MRP/DCP and the need for a tracking table. Expanded the information on repeat use procedure and baseline submissions.
2.5.1 Document Granularity	2.5.1	Included a reference to Annex 3 for consideration when deciding on the level of granularity of Module 3.
2.5.2 File Naming	2.5.2	Included maximum amount of characters for the filename, foldername and total folder. Included reference to eCTD Validation Criteria.
2.5.3 Placement of Documents	2.5.3	Added information regarding the level, the amount and the title of leaves in the submission structure
2.6 Correspondence	2.6	Rewritten partially to clarify which information should and which information should not be included in the eCTD.
2.7 Paper requirements	2.7	Minor change of text, included description of the general need for original signed application form and cover letter. Changed reference to 'Notice to Applicants' into EMA's 'Practical Guide for Paper Submissions'.
2.9.1 File formats	2.9.1	Added information on formats that should not be included in the eCTD structure (MS Word, RTF).

Release Notes for TIGes eCTD Guidance – Comparison of version 2.0 with 1.0

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2.9.2 Portable Document Format (PDF)	2.9.2	Extended the information on use of PDF file versions. Changed the requirement that only PDF version 1.4 should be used to 'version 1.4 or 1.7 should normally be used'. Added information on PDF version 1.3 not being acceptable and the need to explain the use of versions other than 1.4 or 1.7 in the cover letter/explanation note. Updated the information on scanning of wet signatures for the cover letter and application form.
2.9.3 Sequence Numbers	-	Added recommendation to provide tracking table in NP and CP submissions. Included information on resending same sequence in case of technical issues. Moved paragraph on related sequence to separate section.
2.9.4 Related Sequence	-	New section included to provide extensive information on the use of the related sequence, based on Q&A25 and Change Request 20110309-01
2.9.5 Leaf cycle operations	-	New section included to provide extensive information on the use of leaf life cycle operations, based on Q&A23
2.9.6 Bookmarks and hypertext links	2.9.4	Included information on cross-application referencing not being possible.
2.9.7 Node-extensions	-	New section included to provide information on the use of node-extensions, based on Q&A10.
2.9.8 Extensible Mark-up Language (XML)	2.9.5	Removed PIM as initiative to use SML structured information.
2.9.9 Other File Formats	2.9.6	Updated website reference. Extended the information on organization and format of working documents. Updated the example of a folder structure to reflect the situation where working documents need to be submitted to multiple NCA's. Added information on translations being provided outside the eCTD. Added information on format requirement when using e-Mail or Eudralink to send information.
2.9.10 Technical validation of eCTD submissions	2.9.7	Fully rewritten to provide detailed information on new validation criteria (valid as of 01 Sept. 2011) and to remove information of previous validation criteria (Category A, B & C). Included information on how to handle technically valid submissions with incorrect eCTD envelope information. Included information on how to handle historical sequences when supplied to a new NCA.
2.10.2 Security Settings	2.10.2	Changed heading from 'Password Protection' to 'Security Settings'. Included more information on restriction of applying security settings to open any individual file.

Release Notes for TIGes eCTD Guidance – Comparison of version 2.0 with 1.0

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2.10.3 Protection against Malware	2.10.3	Changed heading from 'Virus protection' to 'Protection against Malware'. Minor textual changes to use broader term 'malware' instead of 'viruses'. Removed the need to include confirmation of testing in the cover letter.
2.10.4 Electronic Signatures	2.10.4	Removed reference to Notice to Applications for guidance on the need of signed paper copies. Included instruction to provide signed paper copies where needed (moved this text from 3.2.4 to 2.10.4).
2.10.5 Transmission Media	2.10.5	Combined section 2.10.5 & 2.10.7 and reorganized the information.
2.10.6 Procedure for Sending Electronic Information	2.10.7	Included Eudralink and portals as transmission media. Included information on how to use Eudralink and zipped files. Included preference to provide submissions for workshare /grouping variations together on one CD/DVD. Indicated not to include previously submitted sequences to the same agency on a CD.
2.10.7 Labelling of Media	2.10.6	Included instruction on how to handle too many sequence numbers to list on the CD/DVD label
2.11 Number of Media Requested	2.11	Changed heading from 'Archiving and working copies' to 'Number of Media Requested'. Updated website reference and added reference to Human/Pre-authorisation Q&A23.
2.12 Technical Baseline Applications	2.12	Fully rewritten to expand on information regarding technical baseline applications. Added separate sections 2.12.1 to 2.12.3 to elaborate on the different options.
2.12.1 Baselines Starting as Sequence 0000	-	New section.
2.12.2 Baselines Starting Later in Lifecycle	-	New section.
2.12.3 Re-Baselining a Broken eCTD Lifecycle	-	New section.
3.1 General Information	3.1	Removed eAF and PIM as examples of formats other than PDF.
3.2.2 Creation and Management of Envelope Information	3.2.2	Updated envelope values to reflect M1 specification 1.4 and included a description of each value.
3.2.3 Module 1.0 Containing Cover Letter and Tracking Table	3.2.3	Changed heading from 'Cover letter' to 'Module 1.0 Containing Cover Letter and Tracking Table' and created two sections for information on the cover letter and the tracking table.
3.2.3.1 Cover Letter	-	Reworded this section and removed reference to PIM. Removed instruction to explain omission of submitted data from certain section in the cover letter.

Release Notes for TIGes eCTD Guidance – Comparison of version 2.0 with 1.0

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3.2.3.2 Tracking Table	-	New section to provide information on the use of the tracking table.
3.2.4 Application Forms	3.2.4	Changed heading from 'XML Based Application Forms' to 'Application Forms'. Rewritten text. Provided instruction on operation attribute use. Added that documents that do not fit M2-5 or Response to Questions should be placed in section 1.2.
3.2.5 Product Information	3.2.5	Removed information on PIM. Included instruction to provide RTF or Word files in working documents folder. Indicated there is no need to provide the tracked changes version in PDF, if it is submitted as Word file. Included instruction to manage national translations outside of the eCTD lifecycle. A eCTD sequence is however needed for commission decision documents in the Centralised Procedure.
3.2.6 Use of Response Documents Section	3.2.6	Updated website reference. Modified the location of response documents from 'm1/eu/responses/CC' to 'm1/eu/responses/common'
3.3.2 Structure of Module 2 Documents	3.3.2	Added information on the option to either submit one file or multiple files in the QOS section. Added a reference for submissions covering multiple indications.
3.6.2 Management and Handling of Granular Clinical Study Reports	3.6.2	Reworded the reason for recommending using node-extensions for all clinical study reports. Replaced website reference for reference to section 2.9.7.
3.6.5 Company Core Data Sheet	-	New section
4.1 Initial MA Applications	4.1	Removed table with Procedure type information. Modified example for Centralised Procedure; moved national translations to 'outside eCTD' table and changed the Day Numbers. Included example of Decentralised Procedure
4.2 Variation Applications	4.2	Removed text on cover letter and application form from this section. Added instruction to place documents with no specific CTD location in section 1.2 Application Form. Replaced the table with Submission type information for a website reference. Removed table with Procedure type information. Removed information on baseline (information is in section 2.12). Updated examples of milestones to submit a sequence; moved national translations to 'outside eCTD' table and changed the Day Numbers.
4.3 Extension Submissions	4.3	Changed that extensions can be submitted as a new eCTD application 'depending on the procedure' to 'if a separate lifecycle management is preferred (not applicable in Centralised Procedure)'.

Release Notes for TIGes eCTD Guidance – Comparison of version 2.0 with 1.0

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4.4 Renewal Submissions	4.4	Removed table with Procedure type information. Updated example of milestones to submit a sequence; moved national translations to 'outside eCTD' table and changed the Day Numbers.
4.5 PSURs	4.5	Removed table with Procedure type information. Expanded information on PSURs; included information on work sharing procedures and how to handle new study reports or literature and changes to product information.
4.6 MR and DCP Applications	4.6	Reworded and removed text on cross-referencing to other applications.
4.7.1 Referrals handled through CMDh	4.7.1	Changed heading from 'CMD referral' to 'Referrals handled through CMDh'. Removed table with Procedure type information.
4.7.2 Referrals handled through the centralised procedure	4.7.2	Changed heading from 'CHMP referral' to 'Referrals handled through the centralised procedure'. Removed table with Procedure type information. Reworded text.
4.8 Active Substance Master File	4.8	Partially rewritten. Included references to guidance document and website information on ASMF.
4.10 Plasma Master Files	4.10	Added reference to PMF guidance and information on variations in the 2nd step procedure.
4.11 Applicant Initiated Withdrawals	4.11	Changed heading from 'Applicant Initiated Action' to 'Applicant Initiated Withdrawals'. Removed table with Procedure type information. Included instructions on when and when not to use submission type 'withdrawal'.
4.12 Duplicate Applications	4.12	Included reference to specific requirements for centralised procedure.
Annex 1	Annex 1	Updated website references.
Annex 2	Annex 2	Added prefix 'A2-' to section numbers, e.g. '1.' is now 'A2-1.'
A2-2. Documents that Must Always Be Text Searchable	Annex 2	Removed all bullets on 'This also covers similar documents provided in non-MAA submissions'.
Annex 3	Annex 3	Added prefix 'A3-' to section numbers, e.g. '1.' is now 'A3-1.'
A3-1.1	1.1	Added section 3.2.A attributes to list of Module 3 XML Attributes. Expanded information on exception of 'Manufacturer of Drug Product' section in footnote.
A3-2. General Principle	2.	Added text on general principle (moved from section A3-3.2.2 to here).
A3-2.1 Document Granularity	2.1	Added information to consider the reviewing ability when deciding on a single- or multiple-document approach. Added the use of –var part in filename to differentiate documents.
A3-3.1 Choosing Module 3 XML Attributes	3.1	Provided example on lifecycle issues when changing the Module 3 XML attributes mid lifecycle.

Release Notes for TIGes eCTD Guidance – Comparison of version 2.0 with 1.0

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A3-3.2 Drug Substance (32s) Attributes – Substance-1, Manufacturer-1	3.2	Added that the use of these attributes is mandatory and included reference for guidance.
A3-3.2.1 Drug Substance	3.2.1	Updated website reference.
A3-3.2.2 Manufacturer of Drug Substance	3.2.2	Moved text on general principle to section A3-2.
A3-3.2.2.2 Approach 2 – New XML Sections for Each Manufacturer of the Drug Substance	3.2.2.2	Added example of many manufacturer-specific documents. Added advice against the use of alternative approach to Approach 1 and Approach 2.
A3-3.3 Drug Product (32p) – Product/Dosage Form/Manufacturer	3.3	Added that the use of these attributes is optional and included reference for guidance.
A3-3.3.1 Drug Product Name	3.3.1	Reworded the text on choosing the attributes values.
A3-3.3.2 Dosage Form	3.3.2 + 3.3.3	Added example on deciding on the degree of detail for the dosage form. Included text on strengths (moved from 3.3.3 to here and reworded the text).
A3-3.3.3 Manufacturer	3.3.4	Moved section from 3.3.4 to here.
A3-3.3.3.1 Drug Product Name	3.3.3.1	Reworded partially.
Figure 4 – Approach 1	Figure 4	At 'Note': added an alternative option for the use of the term 'all-strenghts' to avoid issues when submitting a line-extension for an additional strength.
A3-3.3.3.3 Approach 3 – Different XML Sections Covering Each Strength	3.3.3.3	Removed this section.
Figure 6 – Approach 3	Figure 6	Removed this figure.
3.4 Excipients	3.4	Added that the use of these attributes is optional.
A3-3.4.1 Compendial Excipients	3.4.1	Reworded partially.
A3-3.4.2 Non-Compendial Excipients	3.4.2	Added clarification.
A3-3.4.3	-	Added this section to explain on how to handle section 3.2.P.4.5 and 3.2.P.4.6.