Q&A on merging or splitting eCTD lifecycles for different strengths and/or forms of medicinal products

QUESTION 1:

Is it acceptable to combine two earlier submitted separate eCTDs (two or more separate lifecycles) into one eCTD covering several strengths and/or forms of a named product and then continue with a combined lifecycle?

ANSWER:

After justification and agreement with the relevant authority (RMS or NCA), an applicant can combine eCTD lifecycles if this would make presentation of the information in the eCTD for the named product more appropriate.

For example, separate eCTDs were first submitted for each strength/form of the product, but most of the content is common and the applicant therefore wishes to combine them into one eCTD lifecycle to minimize the administrative burden.

The applicant should in this case keep one of the lifecycles (for example the lowest EU procedure number or the lowest strength), **retaining the original UUID**[1], and fill it with the missing contents from the other lifecycles. The other eCTD lifecycle(s) would effectively then be terminated and not used anymore, and all new regulatory activities should be handled in the new, combined, eCTD lifecycle. If there was divergent (dosage form or strength specific) content for the product being merged into the other eCTD, this content should be suitably labelled using leaf titles in the XML of the combined eCTD, to clearly differentiate it from the original content. If there are significant differences in the way the information is presented in the two eCTDs being combined, the applicant may need to consider some harmonization activity within the original eCTD lifecycles before combining them.

The merging should be done before the next regulatory activity for any of the combined products and submitted as the next available sequence, with the **submission type 'none'** and **submission unit type 'reformat'**. It should be clearly stated in the cover letter which products are now included in this combined eCTD lifecycle and which eCTD lifecycle now needs to be archived. Also, it should be stated that there is no new information included, but only a change of the format into one combined eCTD.

Since one or more of the eCTDs is archived and the lifecycle is no longer used, the tracking information for that eCTD(s) is also no longer maintained; the tracking table for the new

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[1] *Footnote: According to the eCTD specification v3.0 and above, all eCTDs must have a valid UUID. The UUID for each eCTD should always be a new, machine generated UUID and it should be created by the eCTD building tool or using an online UUID generator such as https://www.uuidgenerator.net/. The UUID should be kept for the eCTD for its entire lifecycle unless the eCTD is split or merged in accordance with this Q&A. If the eCTD sequence in question does not yet contain UUID, UUID should* ***not*** *be added to an eCTD sequence created prior to the introduction of UUID in accordance with eCTD specification version 3.0.*

combined eCTD should only reflect sequences submitted into that new (combined) lifecycle. Furthermore, a copy of the latest tracking table from the terminated eCTD(s) should also be included in this first combined sequence with the filename(s) *cc-tracking–historical-1.pdf*. The envelope information will also need to be adjusted in the combined eCTD to reflect the new broader scope; there is no need for the applicant to edit previously submitted envelopes in any way.

The next regulatory activity for the named product (all or any of the strengths/forms) should then be submitted as the next available sequence of the combined eCTD lifecycle. For further details, refer to Figure 1 - Merging an eCTD Lifecycle – example.

Please also refer to the *Harmonised Technical Guidance* for *eCTD Submissions in the EU,* on the eSubmission website.

QUESTION 2:

Is it acceptable to split an earlier submitted eCTD covering several strengths and/or forms for a named medicinal product into two or more separate eCTDs and then continue with each separate eCTD lifecycle for upcoming regulatory activities of the respective strength/form?

ANSWER:

In exceptional circumstances and only after justification and agreement with the relevant authority (RMS or NCA), an applicant can split an eCTD lifecycle, if this facilitates further handling of the regulatory activities for the respective strength/form.

For example, several strengths and dosage forms which were first combined into one eCTD lifecycle might need to be separated because the information about the different strengths/forms is now substantially different and difficult to manage in a single, combined eCTD lifecycle.

In this case, the applicant needs to remove some of the information in the existing combined eCTD and resubmit into a new eCTD.

The existing eCTD lifecycle must be maintained for at least one of the strengths/forms and should keep the original UUID. A reformat sequence should be submitted for this eCTD lifecycle to remove the content which is not relevant anymore for this/these strengths/forms using the next available sequence number with the **submission type 'none'** and **submission unit type 'reformat'**. It should be clearly stated in the cover letter which strengths/forms that are now covered by this eCTD lifecycle and which strengths/forms that are moved into new eCTD lifecycles. Also, it should be stated that there is no new information included, but only a change of the format into two or more eCTDs.

The **additional new eCTD** covering the strength(s)/form(s) removed from the original eCTD lifecycle should be created by making **a copy of the original eCTD sequences with a newly**

generated UUID. The applicant then prepares and submits a 'reformat' sequence deleting the content that applies to the strength(s)/form(s) that are still covered by the original eCTD, leaving the documents relevant for this new eCTD lifecycle. This set of sequences that built up the new eCTD would need to be assigned a new UUID, because the UUID needs to be unique.

There may be a technical challenge in some eCTD building tools with creation of a new set of sequences with a different UUID. In such cases, the UUID could be generated outside of the software and added manually in each envelope and the sequences re-imported back into the tool. The new eCTD will then be managed independently from the other split eCTD lifecycles of this named product. For details, see Figure 2 - Splitting an eCTD Lifecycle – example.

Please, also refer to *the Harmonised Technical Guidance for eCTD Submissions in the EU on* the eSubmission website.

If the above option is technically not possible, the applicant, in agreement with the relevant authority (RMS or NCA), could alternatively provide one or more new 0000 sequence(s) with a baseline. This would mean creating a new eCTD with a new sequence 0000 consisting of a baseline sequence with the information for the strengths/forms split off from the original eCTD, with a new UUID. See Figure 3 – New eCTD with Baseline.

For more information on baselines, please refer to section 2.12.1 in the *Harmonised Technical Guidance for eCTD Submissions in the EU*.

Figure 1 - Merging an eCTD Lifecycle – example

Original eCTD No 1 Products 1 & 2	**UUID**	**Description**
0000	not present	Original
0001	not present	Original
0002	12345678	Original
0003	12345678	Original
0004	12345678	Original
0005	12345678	Original
0006	12345678	Original
0007	12345678	Original
0008	12345678	Original

Original eCTD No 2 Product 3	**UUID**	
0000	not present	Original
0001	not present	Original
0002	not present	Original
0003	not present	Original
0004	98765432	Original
0005	98765432	Original
0006	98765432	Original
0007	98765432	Original
0008	98765432	Original

The above two separate eCTDs lifecycles are now merged into one eCTD (lifecycle).

New eCTD lifecycle based on Original eCTD No 1 Products 1 & 2 and now also including Product 3	**UUID**	**Description**
0000	not present	Original
0001	not present	Original
0002	12345678	Original
0003	12345678	Original
0004	12345678	Original
0005	12345678	Original
0006	12345678	Original
0007	12345678	Original
0008	12345678	Original
0009 **(new scope, Product 1,2 and 3)**	12345678	New sequence, Sub Type = None, Unit Type = Reformat, Submission description = Adding content relating to product 3

And stop submitting into the Original eCTD No 2 for Product 3 (It is now terminated.)

Figure 2 - Splitting an eCTD Lifecycle – example

Original eCTD Products 1, 2 & 3	**UUID**	**Description**
0000	not present	Original
0001	not present	Original
0002	not present	Original
0003	12345678	Original
0004	12345678	Original
0005	12345678	Original
0006	12345678	Original
0007	12345678	Original
0008	12345678	Original

One of the products (strength/forms) included in the above eCTD (lifecycle) is now moved into a new eCTD (lifecycle). The original eCTD lifecycle continues for products 1 & 2.

Original eCTD Products 1, 2 only (Product 3 split off to a new eCTD)	**UUID**	**Description**
0000	not present	Original
0001	not present	Original
0002	not present	Original
0003	12345678	Original
0004	12345678	Original
0005	12345678	Original
0006	12345678	Original
0007	12345678	Original
0008	12345678	Original
0009 (new scope, Product 1 & 2 only)	12345678	New sequence, Sub Type = None, Unit = Reformat, Submission description = Removing content relating to product 3

And the applicant also submits a new eCTD lifecycle as below:

New eCTD (copy of Original eCTD, new UUID) and continuing the lifecycle of Product 3 only	**UUID**	**Description**
0000	not present	Original
0001	not present	Original
0002	not present	Original
0003	98765432	Original sequence with UUID in envelope edited
0004	98765432	Original sequence with UUID in envelope edited
0005	98765432	Original sequence with UUID in envelope edited
0006	98765432	Original sequence with UUID in envelope edited
0007	98765432	Original sequence with UUID in envelope edited
0008	98765432	Original sequence with UUID in envelope edited
0009 (new scope, Product 3 only)	98765432	New sequence, Sub Type = None, Unit = Reformat, Submission description = Removing content relating to products 1 & 2

Or, if the above split is not technically possible, a new eCTD lifecycle is started as a baseline:

Figure 3 – New eCTD with Baseline

New eCTD with Baseline, new UUID Product 3 only	**UUID**	
0000	98765432	New sequence, Sub Type = None, Unit = Reformat, Submission description = Separated life cycle for Strength X or Form Y