



CALYX™

Creating US Grouped Submissions

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2 Creating US Grouped Submissions

The following set of procedures provides Best Practice guidance for creating US grouped submissions according to the US Module 1 eCTD v2.3 specification (DTD v3.3).

There are several procedures to perform when creating US grouped submissions:

- Create a Submission Plan
- Create an Initial Assembly Plan
- Publish the Assembly Plan
- Merge the Assembly Plan to the Lifecycles of the Applications
- Create a Subsequent Assembly Plan
- Lifecycle Operations on the Leafs Submitted as Grouped Submission

2.1 Creating a Submission Plan

1. To begin creating a US grouped submission, create a Submission Plan. Using a consistent naming convention for submission plan names will make submission plans easier to find within the system.
2. Identify the applications that will be part of the group and decide which one will be the primary application (the application that will physically contain files submitted as part of the group). Please note that the applications in the group should all have the same application type.
3. Create a submission plan with the same application type as the applications that will be included in the group. The filing type specified during submission plan creation will be used to filter sequences for the association with the submission plan as well as for creating sequences to be associated.

Note: You cannot change **the Submission Plan Type, DTD/Schema, Country, Application Type, or Filing Type** of the submission plan after the submission plan is created.

Create Submission Plan

Submission Plan Name: * Grouped 2253 submission

Submission Plan Code: []

Submission Plan Owner: adminakalenik

Submission Plan Type: * Grouped Submission [v]

DTD/Schema: * us-3-3 [v]

Application Type: * New Drug Application [v]

Filing Type: * Promotional Labeling Advertising [v]

Submission Plan Countries: * Available [] Selected: United States

Submission Plan Status: * Planned [v]

Submission Plan Status Date: * 23-Mar-2015 [calendar icon]

Submission Plan Keywords: []

Submission Plan Description: []

Submission Plan Add Comment: []

- Associate applications that will be part of the group with the created submission plan. Events and sequences can be associated with the submission plan after the applications are associated. However, if this step is skipped, you will be able to create/associate these entities later when merging assembly plans to lifecycles of applications within the group.

Note: If the sequence is associated with the submission plan, you cannot manually create a working assembly associated with this sequence.

2.2 Creating an Initial Assembly Plan

After applications are assigned to the submission plan, you can create an initial assembly plan.

When creating the assembly plan, make sure you have the correct applications in the list of applicable applications. This list can be changed later by updating the attributes of the assembly plan root, but all updates must be completed prior to merging the assembly plan to lifecycles of applications in the group.



The applications listed in this field will be those that will have the lifecycles updated when the assembly plan is merged using the Ready for Submission wizard.



1. Make sure you have the correct XML definitions in the assembly publishing library:



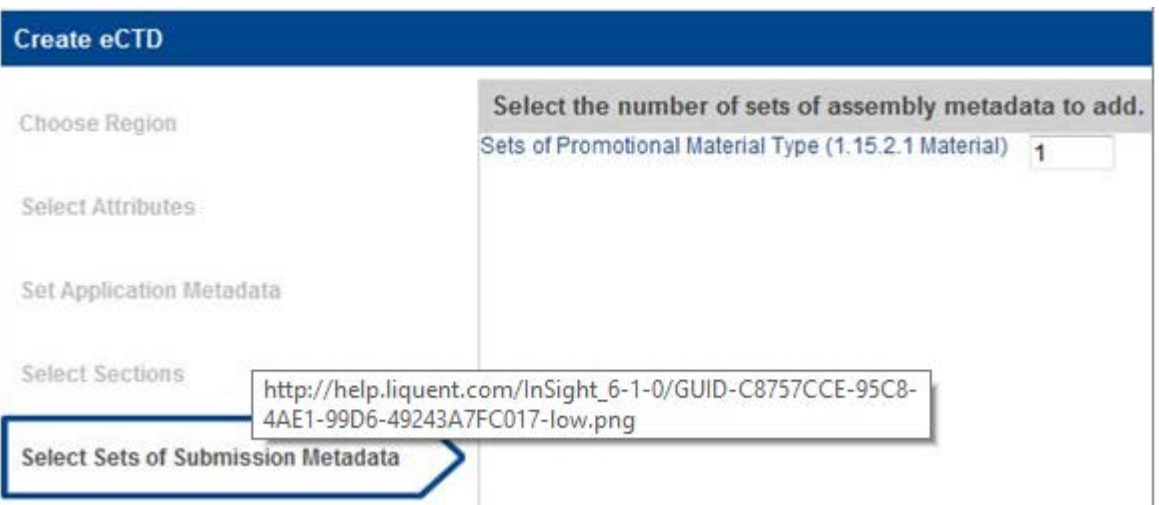
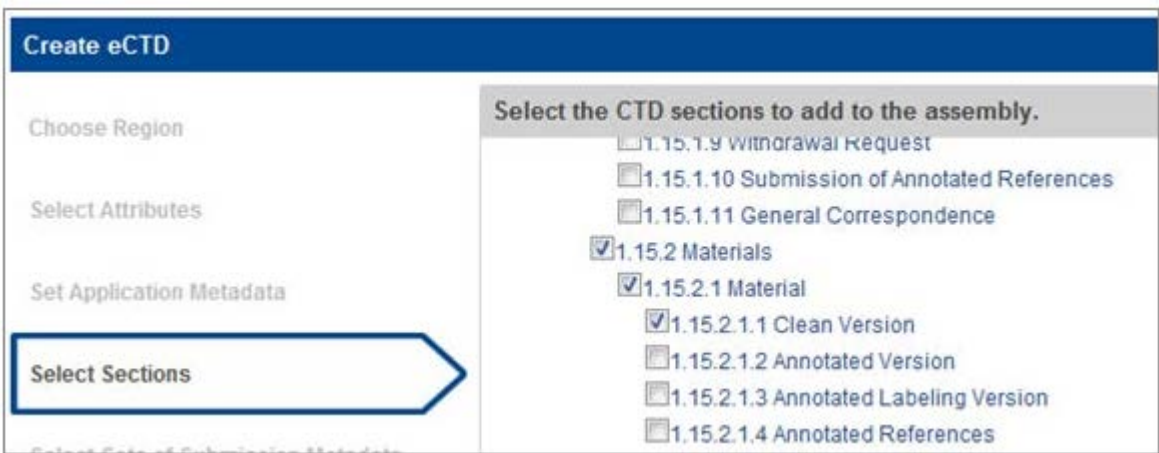
2. Run the Create eCTD wizard to create/update the structure and metadata of the assembly plan. Please note the following when entering eCTD attributes that will be used during publishing:
 - The Application Type should match the Application Type that was specified for the submission plan.
 - The Submission Type should match the Filing type that was specified for the submission plan.
 - The promotional labeling and advertising regulatory contact should be specified for a Promotional Labeling Advertising submission.

3. Within the **Create eCTD** wizard you will be prompted to specify the metadata for the application containing files. Please make sure that the value you enter for the **Application Number** matches one of the values from the Applicable Applications list for the Assembly Plan. The value entered for the **Sequence Number** should match the sequence number of the submission within the primary application.

4. Choose the eCTD sections to be included into the assembly plan. Please note that specific forms must be submitted for the applications of certain types: a form named 1571.pdf is expected for INDs. A form named 356h.pdf is expected for NDAs/ANDAs/BLAs.

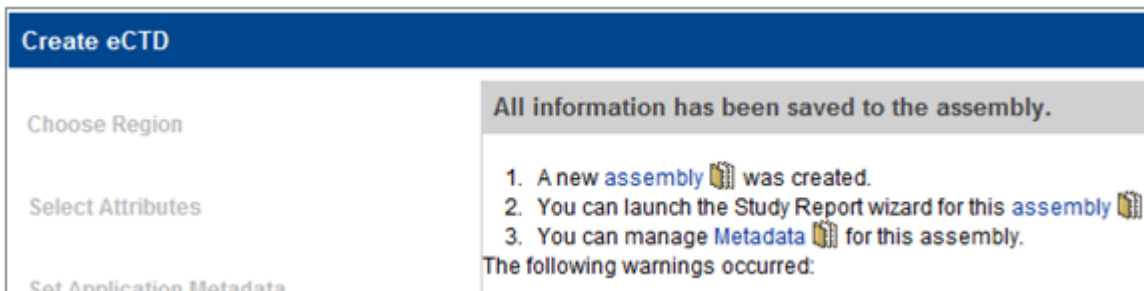


5. If you selected section 1.15.2.1 Material, you will be prompted to enter the number of repeatable 1.15.2.1 sections to be added to the assembly plan, followed by the page, to enter the attributes for each of the sections:

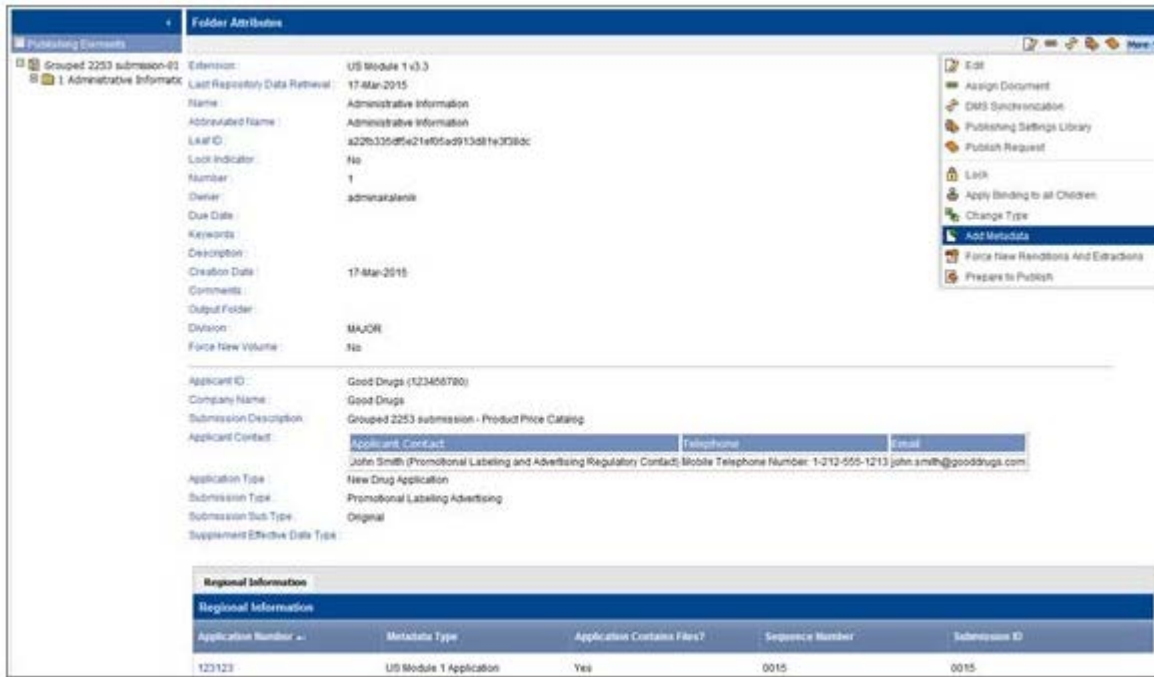




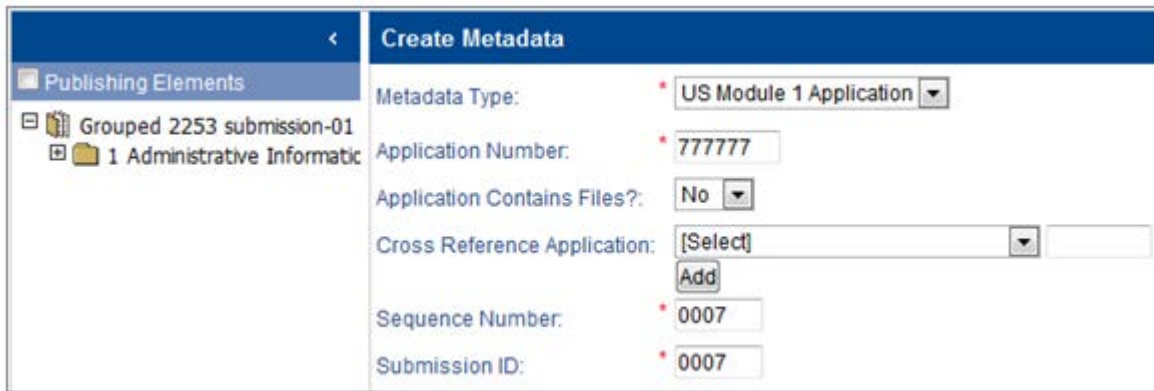
- On the **Summary** page of the Create eCTD wizard you will be prompted to follow the link to manage the Metadata. Select this link.



- This will take you to the folder with the US Module 1 v3.3 extension. Choose the **Add Metadata** menu option to add metadata for other applications in the group:



When adding metadata for non-primary applications, make sure to have Application Containing Files attribute set to No:



- You will be able to see all the metadata added in the Regional Information tab from the folder with US Module 1 v3.3 extension. Any corrections to it may be made by clicking the Application Number hyperlink on the tab:

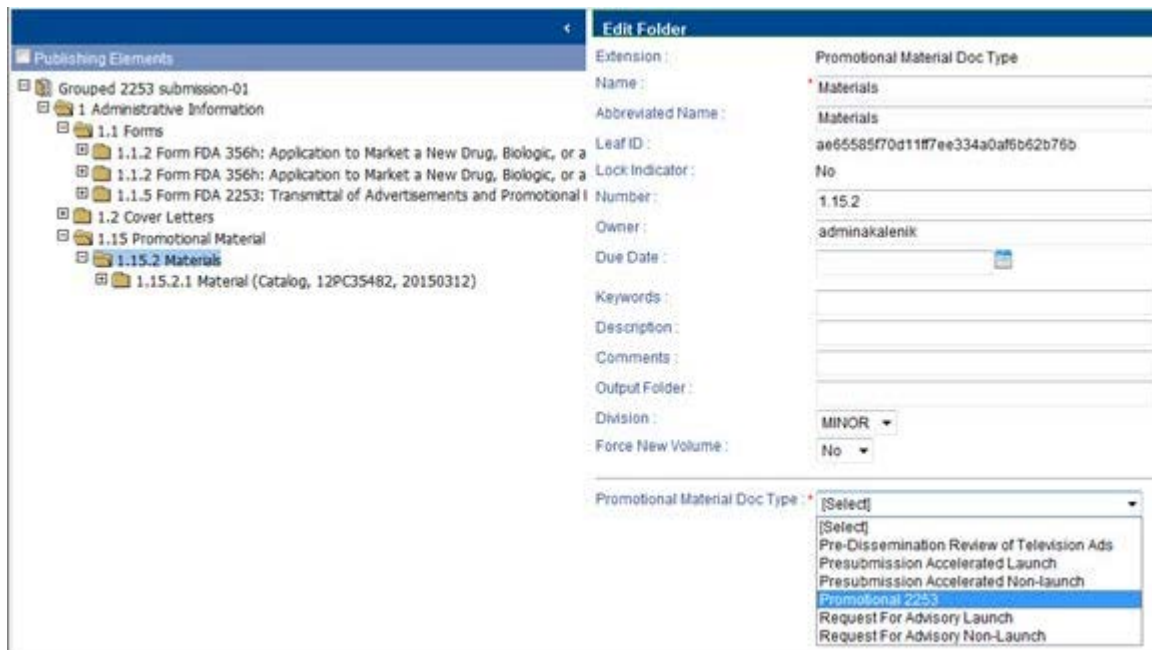


- A separate form 356h or 1571 should be submitted for each application within a group. To update the assembly plan to include separate 356h/1571 forms for each application, browse to the appropriate folder within a structure (1.1.1 Form FDA 1571: Investigational New Drug Application (IND) or 1.1.2 Form FDA 356h: Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use) and choose **Duplicate** from the right-click menu.

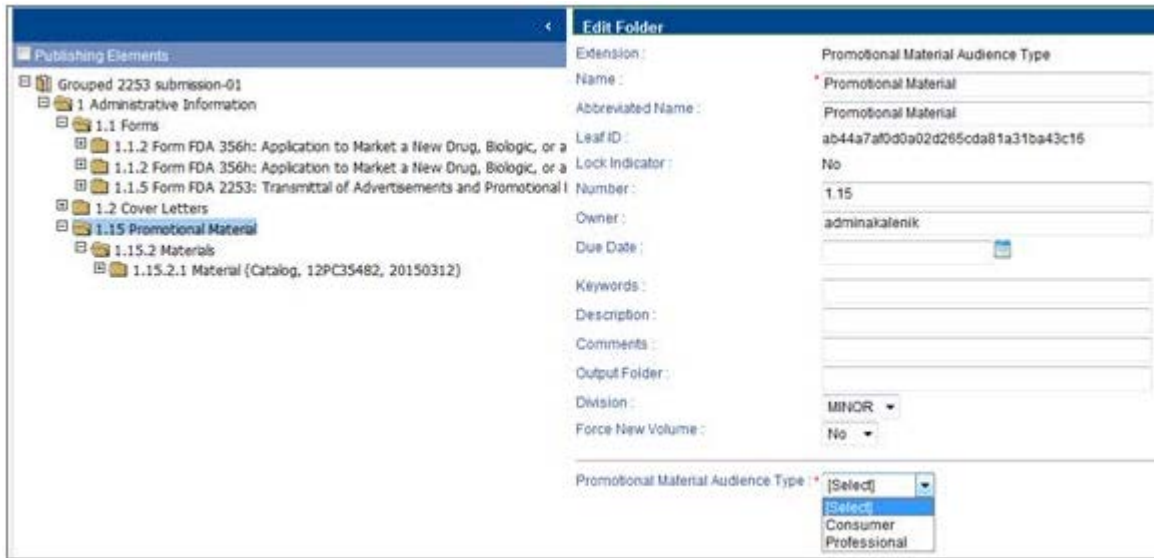
Note: It is recommended that you update the name of the Leaf to include the Application code and Sequence Code that the Leaf is intended for; this will make it easier to locate without having to select each form Leaf.



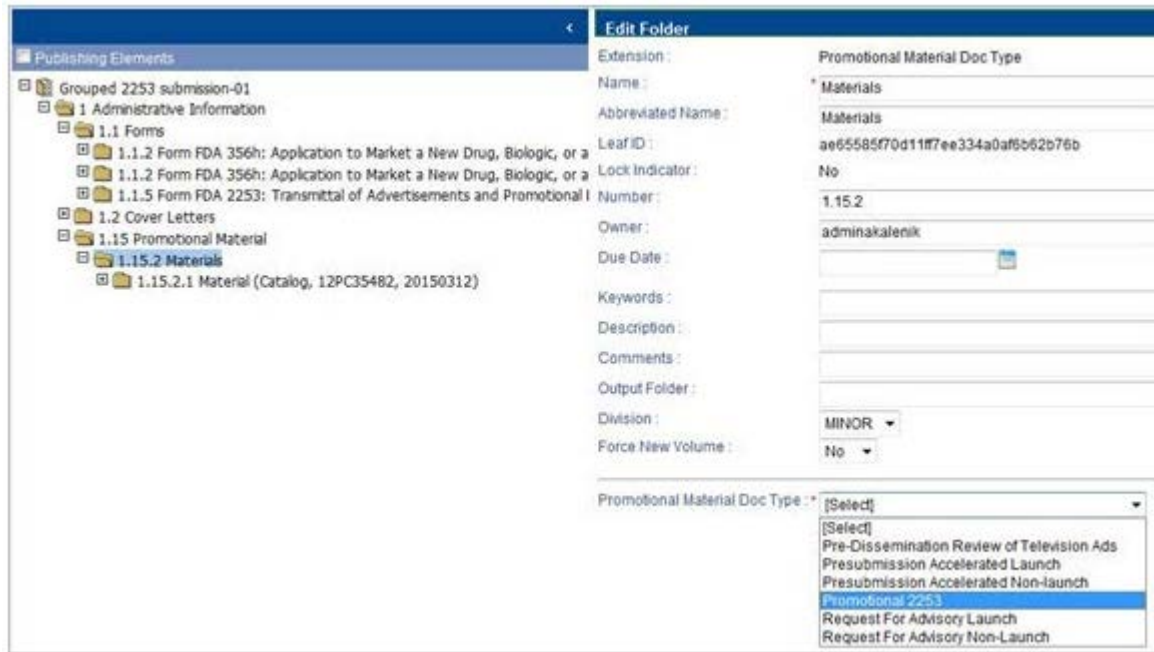
- Edit each form’s folder and set the Application Number extended attribute. The values available are taken from the metadata specified for the assembly plan:



- If any Leafs within the 1.15 section are included, complete the extended attributes on 1.15 Promotional Material section.



12. If any Leafs within the 1.15.2 section are included, complete the extended attributes on 1.15.2 Materials sections.

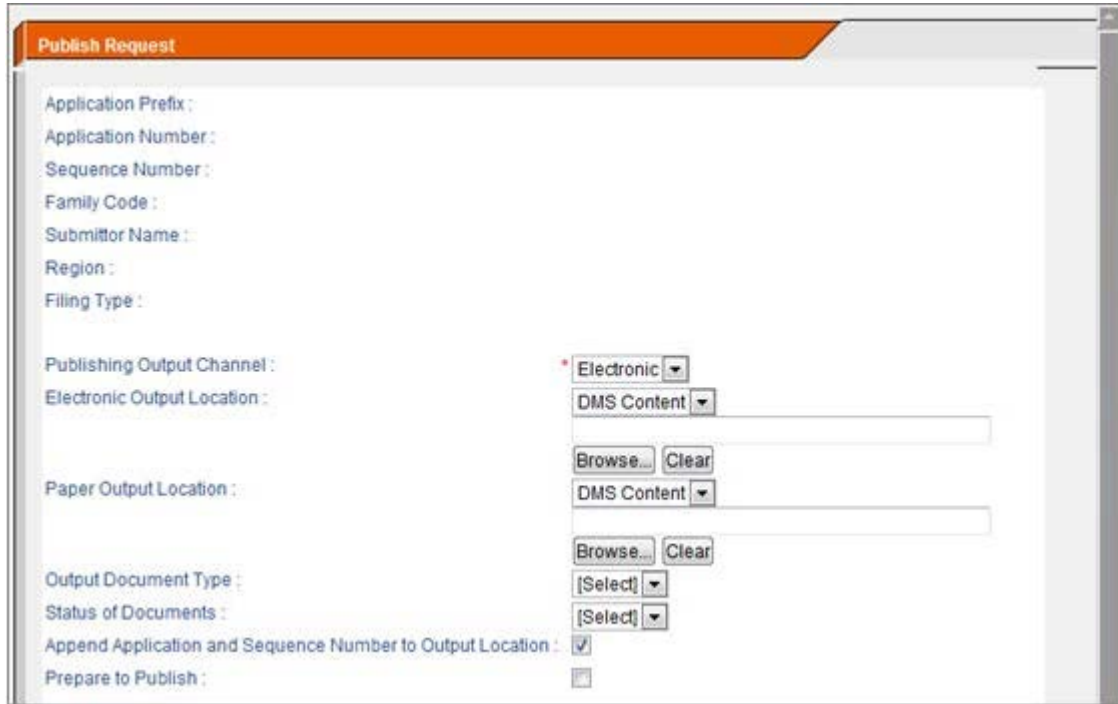


13. Assign source documents to the assembly plan to complete building the structure and content of the submission.

2.3 Publishing the Assembly Plan

It is recommended that you finalize the submission and publish the assembly plan before merging it to lifecycles of applications.

The **Append Application and Sequence Number to Output Location** option will use the Application Number and Sequence Number values from the metadata of the primary application, i.e. *<electronic output location>/123123/0015/*.



Note: When the next assembly plan is created, the metadata is automatically copied from the metadata of the submitted view. This is equal to the metadata of the last assembly plan added to lifecycle. Before publishing the assembly plan, ensure that the metadata is updated with the new Sequence Number. Otherwise, the new output will be published to the same location as the previous one. This may cause loss of data.

2.4 Merging the Assembly Plan to the Lifecycles of the Applications

After the content and structure of the submission are finalized, you must merge it into the lifecycles of the grouped applications by running the Ready for Submission wizard from the corresponding Assembly Plan.

1. The applications that will be affected by the merge will be those listed in the Applicable Applications attribute on the assembly plan root. Make sure the list is correct before running the **Ready for Submission** wizard.

Publishing Elements		Assembly Attributes	
Grouped 2253 submission-01		Submission Plan Name :	Grouped 2253 submission
		Submission Plan Code :	
		Applicable Applications :	123123, 777777

- When the wizard is completed, the Assembly Plan is added to the lifecycle and cannot be changed. However, you can choose whether or not you want individual Sequence Assemblies, which are created by the merge, to be added to lifecycle.
- To ensure that merging with the submitted view content of each application is correct, you need to use the same template and/or naming conventions for eCTD sections. Any folder that was not merged previously from the assembly plan will be merged based on the following criteria matching:

- Name
- Number
- Extension
- Extended attributes

If any of the values listed above are different, the folder will be considered unique and will be merged as new content.

When the merge is successfully completed, there is no synchronization between the source Assembly Plan and the individual Sequence Assemblies created from it. From this point, any changes to the Assembly Plan will not be reflected in the Sequence Assemblies.

- To refresh information from the Assembly Plan, you must manually delete each Sequence Assembly and re-run the **Ready for Submission** wizard against the updated Assembly Plan.

2.5 Creating a Subsequent Assembly Plan

If there is a need to submit a subsequent grouped submission related to the one already submitted, a new Assembly Plan should be created within the same Submission Plan.

Note: Make sure the previous assembly plan is added to the lifecycle before creating a subsequent one.

- Update the metadata and extended attributes with new values:
 - Sequence Number attribute should be updated for all applications within a metadata library.
 - Make sure the Submission Sub Type has the correct value. Certain submission sub-types (application, original, report) can only be submitted once for each regulatory activity.
 - Update Submission Description if needed.
- Update the content and structure of the assembly plan. To be able to perform any operation other than new, the assembly plan that contains the operated leaf should be merged into lifecycles of applications.
- When the assembly plan is ready, it can be published.

4. After the submission is finalized, it must be merged to the lifecycles of applications using the **Ready for Submission** wizard.

2.6 Lifecycle Operations on the Leafs Submitted as Grouped Submissions

If there is a need to perform a lifecycle operation on a leaf that was submitted within a grouped submission, but this operation is not applicable to all the applications within a group, this means that the grouped submission must be closed. You must also close the corresponding Submission Plan. This will unblock operations on such leafs within individual applications.

1. To close the Submission Plan, browse to it and click the Edit Submission Plan icon in the right top corner.



2. On the **Edit Submission Plan** page select the **Closed?** check box and click **Save**.

- After the Submission Plan is closed and individual operations on leafs in the grouped submission were performed outside of the grouped submission (Submission Plan) lifecycle, you cannot reopen the plan and continue the lifecycle within a group. This would cause the lifecycle to be broken within the affected applications.