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CMC Information Relational Map for Module 3

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Purpose

Electronic Common Technical Document (eCTD) is the most desired format for electronic submission of marketing applications (ANDAs, BLAs, NDAs), investigational applications (INDs), and applies equally to original submissions, supplements, annual reports, and amendments to these applications. The Chemistry, Manufacturing and Controls (CMC) information is provided in Module 3 and is the "most granular" technical section of the CTD. Because of the interrelated nature of the section, critical CMC information (for example specification) is discussed throughout the module at multiple places and is either repeated or cross referenced as appropriate. Therefore, when a specific change is made in a particular section of Module 3, it is critical to ensure that the same information is updated in the entire dossier. This is a central theme of good documentation practice for maintaining consistency and accuracy of the information throughout the dossier. However, this is a major challenge for Module 3 because the information is repeated in multiple sections in various contexts and sometimes overlooked and potentially compromising the quality of the submission.

Methods

This poster will provide a CMC-Information Relational Map of Module 3 that outlines CMC keywords of Module 3 and their potential relationship to various sub-sections of Module 3. The Relational Map is derived by key word search of relevant ICH and FDA guidance documents and locating the key words in the Drug Substance (3.2.S) and Drug Product (3.2.P) sections of Module 3.

Results

The resulting information is arranged in a tabular form to be used as a reference document by the regulatory author/team while preparing/reviewing Module 3 of regulatory submissions.

Conclusion

The relational map is expected to serve as a complimentary tool to ensure completeness, accuracy and consistency of Module 3 while making changes to CMC information as part of an original submission or an amendment or supplement

This is a "general map" based on ICH/FDA guidance and it might vary for a given case depending on the company, product and the documentation practice.

Reference

- ICH, The Common Technical Document for Registration of Pharmaceuticals for Human Use: Quality- M4Q (R1) (ICH, September 2002)
- Guidance for Industry: Drug Substance Chemistry, Manufacturing and Controls Information, (Withdrawn)
- Guidance for Industry: Drug Product Chemistry, Manufacturing and Controls Information, (Withdrawn)

Relational Map for Drug Substance (3.2.S.)

Change in eCTD Section		Type of change	Other sections that could be potentially impacted	
3.2.S	Drug Substance		Module 3	Module 2
3.2.S.1	General Information[1]			
3.2.S.1.1	Nomenclature	--	--	--
3.2.S.1.2	Structure	--	--	--
3.2.S.1.3	General Properties	--	--	--
3.2.S.2	Manufacture			
3.2.S.2.1	Manufacturer(s)	Change in information about manufacturer / testing site, responsibilities	3.2.S.2.2., 3.2.S.2.5, 3.2.S.2.6, 3.2.S.4.4, 3.2.S.5, 3.2.S.6, 3.2.S.7.1 and 3.2.S.7.3	2.3.S.2
3.2.S.2.2	Description of Mfg Process and Process Controls	Change in manufacturing process	3.2.S.2.3, 3.2.S.2.4, 3.2.S.2.5, 3.2.S.2.6, 3.2.S.3.2, 3.2.S.7.3	2.3.S.2
3.2.S.2.3	Control of Materials	Change in raw material controls and specifications	3.2.S.4.1 (related because of impurity control strategy), 3.2.S.4.5	2.3.S.2
3.2.S.2.4	Control of Critical Steps and Intermediates	Change in intermediate specifications	3.2.S.2.2, 3.2.S.3.2, 3.2.S.4.1, 3.2.S.4.5	2.3.S.2
3.2.S.2.5	Process Validation	N/A[2]	--	--
3.2.S.2.6	Manufacturing Process Dev.	N/A[2]	--	--
3.2.S.3	Characterization	N/A[2]		
3.2.S.3.1	Structure Elucidation	--	--	--
3.2.S.3.2	Impurities	--	--	--
3.2.S.4	Control of Drug Substance			
3.2.S.4.1	Specification	Change in specification (Addition or deletion of specification, tightening or relaxing of criteria)	3.2.S.4.2, 3.2.S.4.3, 3.2.S.4.4, 3.2.S.4.5, 3.2.S.7.3	2.3.S.4, 2.3.S.7
3.2.S.4.2	Analytical Procedures	Change in analytical proc.	3.2.S.4.1, 3.2.S.4.3, 3.2.S.4.5	2.3.S.4
3.2.S.4.3	Validation of Analytical Proc	N/A[2]	--	--
3.2.S.4.4	Batch Analyses	N/A[2]	--	--
3.2.S.4.5	Justification of Specification	N/A[2]	--	--
3.2.S.5	Reference Std or Materials	Change in reference std	3.2.S.4.2, 3.2.S.4.3, 3.2.P.6	2.3.S.4, 2.3.S.5
3.2.S.6	Container Closure System	Change in container closure system	3.2.S.7.1, 3.2.S.7.3, 3.2.S.2.2, 3.2.S.2.6	2.3.S.6, 2.3.S.7
3.2.S.7	Stability			
3.2.S.7.1	Stability summary and conclusions	Changes in stability summary based on the stability data	3.2.S.7.3	2.3.S.7
3.2.S.7.2	Post approval stability protocol and commitment	Changes to post-approval stability protocol and commitment	3.2.S.7.3	2.3.S.7
3.2.S.7.3	Stability data[3]	New stability data	3.2.S.7.1	2.3.S.7

[1] Typically do not change during product lifecycle
[2] This section is not a point of change initiation. Therefore, this section will only change if there is a change in other section of CMC. Changes made to this section based on changes in other sections should be incorporated in the corresponding Module 2 section
[3] Changes to 3.2.S.7.3 will take place only after the approval of 3.2.S.7.2

Relational Map for Drug Product (3.2.P.)

Change in eCTD Section		Type of Change	Other sections that could be potentially impacted	
3.2.P	Drug Product		Module 3	Module 2
3.2.P.1	Description & Composition of Drug Product	Change in the product description, composition and container closure	3.2.P.2.1, 3.2.P.2.2, 3.2.P.2.4, 3.2 P.4.5, 3.2.P.4.6, 3.2.P.7, 3.2.P.8	2.3.P.1, 2.3.P.2, 2.3.P.8
3.2.P.2	Pharmaceutical Development	N/A		
3.2.P.3	Manufacture			
3.2.P.3.1	Manufacturer	Change in manufacturer /testing site, responsibility	3.2.P.3.2, 3.2.P.3.3, 3.2.P.3.4, 3.2.P.5.4, 3.2.P.7, 3.2.P.8, A.1	2.3.P.3, 2.3.P.4, 2.3.P.8
3.2.P.3.2	Batch Formula	Change in batch formula	3.2.P.2.3, 3.2.P.3.3, 3.2.P.3.4, 3.2.P.3.5, 3.2.P.8.1, 3.2.P.8.3	2.3.P.2, 2.3.P.3, 2.3.P.8
3.2.P.3.3	Description of Manufacturing Process and Process Control	Change in manufacturing process	3.2.P.2.3, 3.2.P.3.4, 3.2.P.3.5, 3.2.P.5, A.1	2.3.P.3
3.2.P.3.4	Controls of Critical Steps and Intermediates	Change in the in-process controls	3.2.P.3.3, 3.2.P.3.5, 3.2.P.5	2.3.P.3
3.2.P.3.5	Process Validation and/or Evaluation	N/A[1]	--	--
3.2.P.4	Control of Excipients			
3.2.P.4.1	Specifications	Change in specifications for excipients	3.2.P.4.2, 3.2.P.4.3, 3.2.P.4.4	2.3.P.4
3.2.P.4.2	Analytical methods	Change in analytical methods for excipients	3.2.P.4.1, 3.2.P.4.3, 3.2.P.4.4	2.3.P.4
3.2.P.4.3	Validation of Analytical Mtds	N/A[1]	--	--
3.2.P.4.4	Justification of Specifications	N/A[1]	--	--
3.2.P.4.5	Excipients of Human or Animal Origin	N/A[1]	--	--
3.2.P.4.6	Novel Excipients	N/A[1]	--	--
3.2.P.5	Control of Drug Product			
3.2.P.5.1	Specifications	Change in drug product specifications	3.2.P.2.5, 3.2.P.5.2, 3.2.P.5.4, 3.2.P.5.6, 3.2.P.8.1, 3.2.P.8.3	2.3.P.5, 2.3.P.8
3.2.P.5.2	Analytical Procedures	Change in analytical proc.	3.2.P.5.3, 3.2.P.5.1, 5.6, 3.2.P.8.3	2.3.P.5, 2.3.P.8
3.2.P.5.3	Validation of Analytical Proc.	N/A[1]	--	--
3.2.P.5.4	Batch Analysis	N/A[1]	--	--
3.2.P.5.5	Characterization of impurities	N/A[1]	--	--
3.2.P.5.6	Justification of specifications	N/A[1]	--	--
3.2.P.6	Reference Std or Materials	Change in Reference Std	3.2.P.5.2, 3.2.P.5.3	2.3.P.5
3.2.P.7	Container Closure	Change in container closure	3.2.P.1, 3.2.P.2.4, 3.2.P.3.3, 3.4, 3.5, 3.2.P.8.1, 3.2.P.8.3	2.3.P.7
3.2.P.8	Stability			
3.2.P.8.1	Stability summary	Changes in stability summary based on the stability data	3.2.P.8.3	2.3.P.8
3.2.P.8.2	Post-approval Stability Protocol and Commitment	Changes to post-approval stability protocol and commitment	3.2.P.8.3 (data will not be changed but ensure that the data is collected according to the change in protocol)	2.3.P.8
3.2.P.8.3	Stability data[2]	New stability data	3.2.P.8.1	2.3.P.8

[1] This section is not a point of change initiation. Therefore, this section will only change if there is a change in other section of CMC. Changes made to this section based on changes in other sections should be incorporated in the corresponding Module 2 section
[2] Changes to 3.2.P.8.3 will take place only after the approval of 3.2.P.8.2

Change in eCTD Section		Type of change	Other sections that could be potentially impacted	
3.2.S	Drug Substance		Sections of Module 3	Sections of Module 2
3.2.S.1	General Information			
3.2.S.1.1	Nomenclature	--	--	--
3.2.S.1.2	Structure	--	--	--
3.2.S.1.3	General Properties	--	--	--
3.2.S.2	Manufacture			
3.2.S.2.1	**Manufacturer(s)**	**Change in information about manufacturer / testing site, responsibilities**	**3.2.S.2.2., 3.2.S.2.5, 3.2.S.2.6, 3.2.S.4.4, 3.2.S.5, 3.2.S.6, 3.2.S.7.1 and 3.2.S.7.3**	**2.3.S.2**
3.2.S.2.2	**Description of Manufacturing Process and Process Controls**	**Change in manufacturing process**	**3.2.S.2.3, 3.2.S.2.4, 3.2.S.2.5, 3.2.S.2.6, 3.2.S.3.2, 3.2.S.7.3**	**2.3.S.2**
3.2.S.2.3	**Control of Materials**	**Change in raw material controls and specifications**	**3.2.S.4.1 (related because of impurity control strategy), 3.2.S.4.5**	**2.3.S.2**
3.2.S.2.4	**Control of Critical Steps and Intermediates**	**Change in intermediate specifications**	**3.2.S.2.2, 3.2.S.3.2 <tbd>, 3.2.S.4.1, 3.2.S.4.5**	**2.3.S.2**
3.2.S.2.5	**Process Validation**	**N/A**	**--**	**--**
3.2.S.2.6	**Manufacturing Process Development**	**N/A[2]**	**--**	**--**
3.2.S.3	**Characterization**	**N/A[2]**		
3.2.S.3.1	**Structure Elucidation**	**--**	**--**	**--**
3.2.S.3.2	**Impurities**	**--**	**--**	**--**
3.2.S.4	**Control of Drug Substance**			
3.2.S.4.1	**Specification**	**Change in specification (Addition or deletion of specification, tightening or relaxing of criteria)**	**3.2.S.4.2, 3.2.S.4.3, 3.2.S.4.4, 3.2.S.4.5, 3.2.S.7.3**	**2.3.S.4, 2.3.S.7**
3.2.S.4.2	**Analytical Procedures**	**Change in analytical procedures**	**3.2.S.4.1, 3.2.S.4.3, 3.2.S.4.5**	**2.3.S.4**
3.2.S.4.3	**Validation of Analytical Procedures**	**N/A[2]**	**--**	**--**

[1] Typically do not change during product lifecycle.
[2] This section is not a point of change initiation. The changes made to this section based on changes in other sections should be incorporated in the corresponding Module 2 section
[3] Changes to 3.2.S.7.3 will take place only after the approval of the CTD.