ICH Q12 - Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

Training Material
Module 5 – Product Lifecycle Management Document

Publication Date: 11 June 2021

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

Legal Notice

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Outline of the Training Material – Chapter 5

- **What is the PLCM document and its purpose?**
- **What are the benefits of introducing the PLCM document?**
- **Submission and maintenance of the PLCM document**
- **Format and location of the PLCM document in MAA**
- **Illustrative example**

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What is the PLCM document and its purpose (1)?

- **The PLCM document is a summary of the following Q12 elements**:
  - ECs
  - Reporting category for making changes to approved ECs
  - PACMPs (when proposed), and
  - Any post-approval CMC commitments
- Supportive information (e.g., development and validation studies) is not part of the PLCM document

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What is the PLCM document and its purpose (2)?

- The PLCM should not contain information which is not already stated elsewhere in the dossier

- Example: Manufacturing Process (Chapter 3.2.2., extract)

  - "An MAH should clearly identify the elements of CMC which they consider to be an EC and those which they consider to be supportive information. The rationales for the ECs are provided in the appropriate CTD modules."

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What is the PLCM document and its purpose (3)?

- “Similarly, the rationales for the associated reporting categories for changes to the ECs should be provided in the appropriate CTD modules.”
- Appropriate modules:

  The background (justification) is mainly in supportive section 3.2.S.2.6/3.2.P.2 and the EC/reporting category is clearly stated in 3.2.S.2.2/3.2.P.3.3. (see *Annex IA* and *IB* for illustrative examples).

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What are the benefits of introducing the PLCM document?

- Serves as a central repository of the ECs, reporting category for making changes to approved ECs, PACMPs, and post-approval CMC commitments
- Enables planning and implementing future changes to ECs in a predictable manner
- Provides transparency and facilitates continual improvement

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Submission of PLCM document

- MAH should submit
  - Their initial PLCM document with the original MAA,

    or
  - In a supplement/variation when the MAH decides to approach the regulatory authority about defining ECs for their already authorised products

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Format and location of PLCM document

- As illustrated in Annex 1F, a tabular format is recommended, but not mandatory
- The PLCM document should be located in Module 3.2R; in some regions (e.g., Japan), it may be placed in Module 1

Maintenance of the PLCM Document (1)

- Maintenance of the PLCM document is an important aspect of product lifecycle management. A PLCM document will lose its purpose if it does not represent the current status of product and process.

Maintenance of the PLCM Document (2)

- The updated PLCM document should be included in post-approval submissions for CMC changes
  - MAH must update the PLCM document when modifying PLCM elements
  - MAH can modify PLCM elements based on knowledge gained over the product lifecycle (e.g., adding/reducing ECs, or modifying reporting category of ECs)

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Maintenance of the PLCM Document (3)

- Example: Revision of Approved ECs (Chapter 3.2.4)
  - "It may be necessary to change approved ECs as a result of knowledge gained during the product lifecycle (e.g., manufacturing experience, introduction of new technologies or changes in the control strategy)."
- MAH should follow regional expectations for maintaining a revision history for the PLCM document

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CTD Section	Established Condition *(Identification & Justification of EC is presented in the relevant section of CTD)*	Reporting Category *When Making a change to the Established Condition*
3.2.S.4.1	**Input Material** – API PSD (5-200 um)	Tighten (NL) Widen (NM)
3.2.P.3.1	**Drug Product manufacturing sites** *(Including those for testing, primary and secondary packaging, device assembly for drug-device combination products)*	
3.2.P.3.2	**Drug Product Batch Formula** *(Qualitative & Quantitative)*	
3.2.P.3.3	The **manufacturing process** consists of the following sequence of unit operations: *1. Powder blending* *2. Roller compaction* *3. Tablet compression* *4. Film-Coating*	
	1. Powder blending *The active substance and three excipients are mixed together. The following process parameter are defined as ECs.*	
	Operating principle: *Diffusion mixing*	**PA**
	Equipment type: *V-Blender*	**NL**
	Scale: *200 Kg*	**NL**
	Design space for blending process parameter • *Blend speed: 10-20 rpm* • *Blend time: 15-25 minutes*	**NM**
	2. Roller compaction	
	3. Tablet compression	
	4. Film-coating	
3.2.P.3.4	**Design space for blending process parameter** • *Blend speed: 10-20 rpm* • *Blend time: 15-25 minutes*	**NM**
3.2.P.4	Input Material: Excipient #1 Specification *(Pharmacopeial)*	
3.2.P.4	Input Material: Excipient #1 Specification *(Pharmacopeial)*	
3.2.P.4	Input Material: Excipient #1 Specification *(Pharmacopeial)*	

Illustrative Example: Annex I F

This example for drug product illustrates how MAH can present the elements of ICH Q12 Chapter 5 in an initial PLCM document. Other approaches and formats can be used as appropriate. This example follows the 'enhanced parameter-based approach' from Annex IA; example for identifying Established Conditions for a Solid Dosage Form Tablet X (small molecule).

CTD Section Referenced	PACMP or Post-Approval CMC Commitment (If applicable)
3.2.P.3.3	PACMP included in the MAA for expanded range for scale
3.2.P.3.3	CMC Commitment to monitor dissolution performance for 10 batches manufactured at upper end of blend time range due to potential over lubrification at the proposed commercial scale (200kg)