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

Training Material
Module 2 – Categorisation of post-approval CMC changes

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Legal Notice

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Categorisation of post-approval CMC Changes

Objective of Categorisation:

- Advise/inform what regulatory action is expected in case of a post-approval change
- Provide a communication tool between regulator and MAHs for managing post-approval changes based on potential risk; this includes:
  - Nature of the change
  - Conditions and documentation associated
  - Reporting category
  - Time frame for evaluation and/or implementation

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Rationale

- CMC changes vary from **low to high potential risk** with respect to product quality, safety, and efficacy
- This process of regulatory communication should be commensurate with that potential risk
- Based on nature and potential risk of the change, an inspection may be needed

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Guiding Principles (1)

- This chapter describes a framework that encompasses a risk-based categorisation for the type of communication expected of the MAH with the regulatory authority regarding CMC changes. Such framework would include the following categories for regulatory communications with one or more levels in each case:
  - **Prior-approval:** Changes with sufficient risk to require regulatory authority review and approval prior to implementation
  - **Notification: Moderate- to low-risk changes** that do not require prior approval and generally require less information to support the change

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Guiding Principles (2)

- In addition, the changes that are not required to be reported to regulators are only managed and documented within the PQS but may be verified on routine inspection by regulators.
- It should be noted that all changes, regulatory or not, have to be managed under a PQS.

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- **Reporting category and terminology**
  - requesting prior approval from the regulatory authority,
  - notifying the regulatory authority, or
  - simply recording CMC changes

ICH Terminology		Example of Regional Terminology	Risk level
Prior Approval (PA) Changes with sufficient risk to require regulatory authority review and approval prior to implementation		PAS, Type II, PCA, etc.	High
Notification* Moderate- to low-risk changes that do not require prior approval and generally require less information to support the change	**Notification Moderate** (NM)	CBE 30, Type IB, MCN, etc.	Moderate
	Notification Low (NL)	CBE 0, AR, Type IA, MCN, etc.	Low
Recording change that are not required to be reported only managed and documented within the PQS, but may be verified on routine inspection	**Not Reported** (NR)		Negligible

* These changes are communicated to the regulatory authority as a formal notification that takes place within a defined period of time before or after implementation, according to regional requirements.

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Conclusion

- To achieve the objectives of product lifecycle management as described in ICH Q12, an important step is to **establish a risk-based categorisation of post-approval changes.**

- Regulatory authorities are encouraged to utilise such system as it promotes **transparency and predictability** for both Industry and Regulators.