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Note on EU implementation of ICH Q12 (guideline on technical and regulatory considerations for pharmaceutical product lifecycle management)

This explanatory note is published in parallel to the ICH Q12 Step 5 guideline (EMA/CHMP/ICH/804273/2017) and annexes (EMA/CHMP/ICH/831751/2017) which were adopted by CHMP in January 2020.

The ICH Q12 guideline provides regulatory tools and enablers with associated guiding principles, which are intended to harmonise globally the management of quality related post-approval changes. Some of its principles have been inspired by the current EU legal framework on variations.

The ICH Q12 guideline puts forward a risk-based approach that includes a certain amount of flexibility in making post-approval changes as regards the quality of the product. The EU legal framework on variations also provides for a risk-based approach, and any flexibility it provides follows directly from the specific provisions that are set out in this framework. As a result, there are some conceptual differences between ICH Q12 and the EU legal framework which have an impact on how the full operational and regulatory flexibility as laid down in the ICH Q12 guideline can be implemented in the EU.

Given that the level of flexibility in different ICH regions tends to vary depending on the respective legal frameworks, the ICH Q12 guideline explicitly states that its adequate implementation will depend on the applicable regulatory framework in place.

Several of the tools and concepts foreseen in the ICH Q12 guideline are considered compatible with the EU legal framework on variations and some even stem directly from this framework. These tools and concepts can already be applied, as such, by industry by following the current EU variations framework. In other words, no particular actions are required in the EU in order to implement these parts.

Moreover, the ICH Q12 guideline establishes a harmonised approach to defining which elements in an application are considered necessary to assure product quality and therefore would require a regulatory submission if changed post-approval. The ICH Q12 guideline refers to this required or necessary information as 'Established Conditions' (ECs). While this term does not exist in the EU variation legal framework, generally speaking, Established Conditions mirror information and quality

characteristics that are subject to a variation, as described in the EU Variation Regulation (EC) No 1234/2008 (as amended) and associated EU Variation Guidelines¹.

However, additional scientific risk-based approaches to defining Established Conditions and associated reporting categories, as described in Chapter 3.2.3, and the Product Lifecycle Management (PLCM) Document, as described in Chapter 5, are not considered compatible with the existing EU legal framework on variations.

It is important to note that the legal framework always takes precedence over technical and scientific guidelines. More specifically this means that the definition of Established Conditions and their reporting categories must follow the requirements laid down in the current EU Variations Regulation and associated EU Variations Guidelines. With respect to the Product Lifecycle Management (PLCM) document, in case such a document is submitted, it cannot be currently recognised in the EU due to the fact that it is not referred to in the EU legal framework.

With regard to Chapter 6 “Pharmaceutical quality system (PQS) and change management” and Chapter 7 “Relationship between regulatory assessment and inspection”, while the expectations on industry and regulators are broadly in line with current practice in EU, some additional clarifications regarding demonstration and evaluation of PQS effectiveness and communication between regulators will require further consideration during implementation of the guideline.

Irrespective of the above, the tools and concepts in the ICH Q12 guideline that are not foreseen in the EU legal framework will be considered when this framework will be reviewed. In the meantime, the European Commission, together with the EMA and the National Competent Authorities, will continue to work on the implementation of the ICH Q12 guideline within the existing EU legal framework.

European Commission
Directorate-General for Health and Food Safety

European Medicines Agency

¹ Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures (2013/C 223/01)