European Federation of Pharmaceutical Industries and Associations

EFPIA/VE Final Response to DG Sante Call Comments on Revision of EU Variations Framework

EFPIA/Vaccines Europe fully support revision of the EU variations framework and agree with the stated aim of this first step to streamline procedures and ensure better handling based on a science and risk-based approach. We are encouraged to see the inclusion of the following changes: Removal of the default type II classification for quality/manufacturing changes for biological products, including advanced therapies; formalisation of the legal basis for use of existing additional regulatory tools; extension of influenza vaccines approaches to coronavirus vaccines; and reference to annual updates for minor variations whilst retaining the flexibility of immediate submission in some cases, which is critical. These proposals are encouraging steps to a more efficient framework which may be fully realized after the update to the general pharmaceutical legislation. Following review of the draft regulation, EFPIA/VE offers feedback on the following points, with some additional details included in the separate appendix: 1) Classification guideline review: the proposal for annual reports by the Agency is generally welcomed and offers the opportunity for more regular adaptations. However, it is unclear how quickly the EC will implement the changes to the guideline and whether the scope includes changes to accommodate scientific and technical progress other than new recommendations under Article 5. We encourage the EC to be ambitious here and aim for clear, regular updates that broadly encompass all necessary revisions. Ultimately, our view is that EMA/HMA should have full accountability for managing and updating the classification guideline. 2) Additional regulatory tools: The wording in Article 6a is unclear and could be expanded to enable the introduction of Established Conditions and PLCM as further regulatory tools. We suggest additional qualification to the Article as follows 'specific regulatory tools e.g., design space, post approval change management protocols and others as science and technology progresses.' 3) Super-grouping: The introduction of this concept into the regulation is fully supported, but the related proposed revision to Article 7(2) lacks clarity. Since this Article now appears to apply only to minor/type IA variations for single marketing authorisations (MA) under the same MA holder it could be revised to 'where multiple minor variations to the terms of the same marketing authorisation owned by the same holder...'. 4) Worksharing: this now appears mandatory for certain cases (Article 20(1)) but MA holder choice may be warranted e.g., in justified cases.

Regarding the annexes, we believe the proposed change to Annex I, point 1(c) is unclear and would keep the wording in the original Annex I ('efficacy and/or safety'). Generally, for Annex II we believe that there is an opportunity to move much closer to the aims of ICHQ12 by replacing the detailed text describing the classification of variations with general principles, and that this should actively be considered at step 1. However, should this not be possible, we offer the following feedback: 1) Introduce additional text at the start of Annex II 'A variation whose classification is not determined by a product lifecycle document agreed by the relevant authority shall be classified as follows:' 2) Clarify changes for point 1(f) which appears to be unchanged. 3) Revise point 2(f), to only reference introduction of a design space as a type II variation where this 'may have a significant impact on the quality, safety or efficacy of the medicinal product.' 4) Revise points 1(g) and 2(n) to clarify their application to changes in medical devices that impact the use of medicinal products, whilst in vitro diagnostics follow a separate process and should be excluded. Finally, under Annex III, further amendments could be made to allow grouping of parallel (i.e., concurrent but non-consequential) type IB and type II variations, to the same Module 3 section.