19 September 2023

To: European Commission
SANTE - DG Health and Food Safety

From: The International Society for Pharmaceutical Engineering (ISPE)
Transparency Register 316626227774-56

RE: ISPE response to European Commission Call for Evidence: Pharmaceuticals—for changes to marketing authorisations (Revision of the variation framework for medicines)

General Comments

ISPE strongly supports the purpose of this Initiative, that is to make the post-marketing lifecycle management of medicines more efficient, by reducing the administrative burden for the pharmaceutical industry and making better use of regulatory authorities' resources.

ISPE recognises that this Initiative is a short-term solution under the existing legislation and is needed to streamline resources for regulatory authorities and Marketing Authorisation Holders (MAHs) and speed up the authorisation of variations pending reform of EU pharmaceutical legislation.

ISPE suggests that this Initiative considers:

1. Fully implementing ICH Guideline, Q12, Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management.
2. Introducing concepts of work sharing and mutual reliance not only within the EU but also with agencies outside the EU.
3. The global implications of introducing new regulatory process and procedures.

Background and support for these suggestions are given below.

1. ISPE recommends that as part of this Initiative, the European Commission considers fully implementing ICH Guideline, Q12, Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management alongside the modified current variations procedures. This could be achieved by reconsidering how current EU legislation could be interpreted to allow implementation of science- and risk-based concepts as discussed in ICH Q12 (e.g., Established Conditions), and outlined in the Note on EU Implementation of ICH Q12, (EMA/CHMP/ICH/78332/2020). Alternatively,

consideration could be given to making relatively minor amendments to current EU legislation. This Call for Evidence document does infer that minor changes to current legislation may be agreed.

The objectives of ICH Q12 are fully aligned with this Initiative.

Additionally, full implementation of ICH Q12 would:

- support a purpose of this Initiative, which is to extend the risk-based approach to variation categorisation to certain biological medicinal products and to update, in particular, the rules on biological medicinal products and changes to active substances.
- Increase efficiency for MAHs especially those MAHs supplying biological products to patients globally.

2. ISPE suggests that this European Initiative considers introducing in revised variations legislation concepts of work sharing and mutual reliance between agencies within and outside the EU as proposed by the International Coalition of Medicines Regulatory Authorities (ICMRA) in their Pharmaceutical Quality Knowledge Management System project (https://www.icmra.info/drupal/sites/default/files/2023-08/icmra_industry_pqkms_ws2023_presentations.pdf). Mutual reliance and improved regulator engagement are major learning points and successes from the Covid pandemic.

3. ISPE also suggests that this Initiative considers the global implications of new EU regulatory process and procedures to avoid additional burden, complexity, and uncertainty of regulatory outcome for MAHs when filing a post approval change to multiple agencies.

   ISPE has undertaken an initiative, *Enabling Pharmaceutical Innovation: Delivering for Patients*, and as part of this initiative is conducting a survey to understand the extent and magnitude of challenges/barriers to developing and implementing innovative technologies globally. Although not specifically directed at the EU situation, preliminary responses show that regulatory challenges are significant factors influencing decisions to proceed with innovations. Many, but not all innovations are progressed as continual improvement opportunities using the post approval/variations regulatory pathway, and many of these proposed innovations are submitted to multiple regulatory agencies. Companies have provided feedback in the ISPE survey that differences in regulatory requirements are a major challenge to implementation of new technology. ISPE is prepared to share the output of the survey with EMA.

In addition to the above considerations for this Initiative, ISPE suggests that the European Commission, as part of the proposed reform of EU pharmaceutical legislation, considers introducing an annual reporting procedure. Such a procedure could be applied to low risk and technical/administrative post approval changes leading to increased communication efficiency.

We appreciate the opportunity to submit these comments for your consideration. Please do not hesitate to contact me if you have any questions.

Respectfully,

Thomas B. Hartman, ISPE President and CEO
thartman@ispe.org

cc: Michael L. Rutherford, ISPE Chairman