7 July 2020

ISPE Response to the EC Pharmaceuticals – safe and affordable medicines (new EU strategy) Roadmap

ISPE acknowledges the significance and timeliness of the *'EU Pharmaceutical Strategy - Timely Patient Access to Affordable Medicines'* issued on 03 June 2020.

The International Society for Pharmaceutical Engineering (ISPE) acknowledges the significance and timeliness of the *'EU Pharmaceutical Strategy - Timely Patient Access to Affordable Medicines'* issued on 03 June 2020 and would like to respond as an industry association to the Roadmap. ISPE would welcome being engaged as part of the "Additional consultations" process as a stakeholder with significant technical expertise and a broad portfolio of relevant projects. We believe ISPE is uniquely positioned to provide impactful insights to the problems the strategy seeks to address, specifically on availability of pharmaceuticals to patients, the benefits of digital and emerging science and technology, and better regulation. The problems the roadmap outlines strike a chord with ISPE, it aligns with many of the industry- and regulator-led initiatives ISPE has been working on for many years.

A summary of ISPE projects and programmes relevant to the proposed specific objectives of the EU Pharmaceutical Strategy are given below with relevant ISPE programmes and projects highlighted in bold text.

Ensure greater access and availability of pharmaceuticals to patients

ISPE commenced a **Drug Shortages Initiative** globally in 2013 and has continued to focus on the technical, scientific, manufacturing, quality and compliance issues associated with a company's supply chain, related to its ability to source, manufacture and distribute products that have resulted in drug shortages. ISPE's research was cited in the USFDA's Strategic Plan for Preventing and Mitigating Drug Shortages. That and subsequent research has been published by ISPE in its *Drug Shortages Prevention Plan*, the *Drug Shortage Gap Assessment and Prevention Tool*, and the *Report on Drug Shortages* developed in conjunction with the Pew Charitable Trusts. ISPE's *Drug Shortages Prevention Plan* formed part of an inter-association task force's collaborative plan - developed at the request of the EMA - for the prevention of drug shortages resulting from manufacturing quality issues. ISPE's continues to provide platforms for dialog between the different sectors of the pharmaceutical industry and global health authorities related to drug shortages.

The current COVID-19 highlights the necessity to focus on drug shortages, expanding the lens to **business continuity planning**. The EU Pharmaceutical Strategy Framework gives us the opportunity to effectively address the complex and multi-faceted issues contributing to drug shortages that require close technical collaboration and clear communication between the pharmaceutical industry and global

health authorities. ISPE has been instrumental in facilitating communication between the different sectors of the pharmaceutical industry and global health authorities related to drug shortages. Additionally, the **ISPE Drug Shortage Prevention Plan** and **Drug Shortage Assessment and Prevention Tool** facilitate business continuity planning, communication with the authorities and proposed risk mitigation options.

ISPE excels in providing guidance on technology solutions which may be invaluable in averting shortage situations: **continuous manufacturing**, emerging novel products and **facility technology developments** such as manufacturing pods, emerging manufacturing, small volume/flexible specialty manufacturing…etc.

ISPE has had a long-standing commitment to mitigating and preventing drug shortages and looks forward to sharing the outputs of our industry-led programs that are appropriate inputs to the EU Pharmaceutical strategy.

Enable innovation including for unmet medical needs in a way that harnesses the benefits of digital and emerging science and technology and reduces the environmental footprint

ISPE efforts on **Pharma 4.0™** align with this objective. Pharma 4.0™ is a readiness map for future digitization and innovation for novel technology and the continual improvement of existing technology. Digitization is an important component of Pharma 4.0™, which will connect everything, creating new levels of transparency and speed for digitalized manufacturing. This will enable faster decision-making and provide in-line and in-time control over business, operations, and quality. It will also require higher levels of security, since connected systems heighten vulnerability.

The ISPE's **Product Quality Lifecycle Implementation (PQLI)®** initiative directly relates to the roadmap. It endeavours to '*build a holistic, patient-centred, forward-looking EU Pharmaceutical Strategy which covers the whole lifecycle of pharmaceutical products from scientific discovery to authorisation and patient accesses'*. PQLI provides guidance on practical implementation of the concepts described in the ICH guidelines, focusing on Q8, Q9, Q10, Q11 and Q12 and associated regional guidance to help ensure product quality throughout a product lifecycle, leading to continual product improvement. We feel the necessity to develop solutions, which are part of the EU strategy to cover emerging regulatory and scientific topics related to CMC and GMP approaches to ensuring product quality, inclusive of **Continuous Manufacturing**, **ICH Q12 Implementation**, **Knowledge Management**, **Patient Centric Quality Standards** and **Process Validation**.

Better Regulation

In addition, ISPE believes it could engage in the challenge “Technological and scientific developments may challenge the regulatory framework and consequently lead to unintended barriers to needs-driven innovation” and hence produce “Better Regulation”.

ISPE strives to facilitate industry-wide clarity of new regulations and guidance’s, develop positions that provide solutions to reconcile global regulatory challenges and advocate for convergence of regulatory expectations including mutual reliance for inspections of manufacturing facilities and harmonisation of pharmacopeia standards and monographs. Whilst not explicitly stated in the roadmap, we believe reconciling global regulatory divergence is critical to reduce redundancy and address the challenge of adhering to diverse and often conflicting and non-scientific regulatory requirements.

An example of ISPE’s breadth of technical expertise was the comprehensive and thoughtful response to PIC/S regarding Annex 2A Manufacture of **Advanced Therapy Medicinal Products** for Human Use. At the request of the PIC/S rapporteur, supplementary recommendations were given by ISPE-led teams of experts on applicability of GMP in processes for manufacture of messenger RNA products and on DNA-based products.

In accordance with “Better Regulation” the ISPE has assumed leadership in **Advancing Pharmaceutical Quality (APQ).** The basic framework of the ISPE APQ program is to “assess, aspire and act” on quality maturity. ISPE will publish this year the first of a series of Good Guidance Practices on an industry-led Quality Maturity Framework, based on ICH Q10, which could be leveraged by industry and potentially the EU. This will enable and foster industry ownership of quality beyond compliance and Integrate quality, cultural, and operational excellence principles and learnings and ultimately increase reliability of supply for quality product. Building these principles into the EU Pharmaceutical strategy or an associated document would be deemed to be hugely advantageous.

We would recommend that the Roadmap and strategy considers embracing the concept of improving **Quality Culture** in Pharmaceutical Manufacturing facilities. Quality Culture has always been important within pharmaceutical manufacturing operations. Recently health authorities have placed additional emphasis on Quality Culture by including it in guidance documents and inspection protocols such as PIC/S Data Integrity Guidance, FDA New Inspection Protocol Project (NIPP), and MHRA Data Integrity Guideline. The influence of an organization’s Quality Culture is acknowledged as a key enabler for ensuring product quality. Cultural excellence requires that all employees in the pharmaceutical supply chain are passionate about eliminating errors by making quality their driving principle. ISPE’s have developed in its Cultural Excellence Report a collection of practical, powerful tools and a comprehensive behaviour-based approach for improving quality culture as a means of delivering enhanced quality and business outcomes. We look forward to integrating the learnings of the Quality Culture and Excellence programs into our detailed responses on the EU strategy.

Conclusion

The EU roadmap to improve and accelerate patients’ access to safe and affordable medicines and to support innovation in the EU pharmaceutical industry is welcomed as an important dialogue with Industry. It will help address a holistic lifecycle approach for medicines from R&D to authorisation and patient access, it should address the many lessons learnt from COVID-19 on how to better prepare for

future pandemic with robust regulatory framework and supply chain. The COVID-19 pandemic has taught the pharmaceutical manufacturing community a lot - the rapid development of Guidances, remote inspections and the dynamism of the Regulators and industry to maximise manufacturing capability. ISPE looks forward to engaging on the EU strategy and helping to 'future proof' our industry and the patients we need to serve.

With regard to next steps, ISPE recommends that representatives of the EU Commission contact Dr Thomas Zimmer, Vice President ISPE European Operations.