



## ISPE Response to MHRA's Consultation on Point of Care Manufacturing (published 12 Aug 2021)

### **ISPE General Comments:**

ISPE applauds MHRA for their forward-thinking consultation on Point of Care (POC) manufacturing. ISPE, a not-for-profit association with members representing the entire pharmaceutical lifecycle, and is the global industry leader in connecting pharmaceutical knowledge to deliver manufacturing and supply chain innovation, operational excellence, and regulatory insights to enhance industry efforts to develop, manufacture and reliably deliver quality medicines to patients. As part of delivering our mission, ISPE has established a Portable and Point of Care Working Group of subject matter experts under the umbrella of ISPE Product Quality Lifecycle (PQLI)<sup>®</sup> Initiative. ISPE would welcome further discussion or interaction with MHRA on this topic outside of the boundaries of this consultation.

ISPE is greatly encouraged to see proactive and supportive legislation to enable a spectrum of manufacturing options. Aspects of the proposed regulatory framework that ISPE finds to be particularly helpful to enable POC Manufacturing (and possibly other manufacturing on the spectrum from fixed large-scale to home-based) are as follows:

- Provisions for control site based qualified person (QP) oversight
- Risk based frequency of inspections for the control and POC sites
- Flexible data requirements for finished product testing, batch analyses, stability testing and labeling dependent on the nature of the product and shelf life
- Adaptation of CTA/MAA requirements to not specify each individual manufacturing site.

ISPE's recommendation for the new framework is that it should not be limited in scope to cases where the current manufacturing model is not feasible (as discussed in the introduction). While we do not think that point of care or mobile manufacturing will fully replace current centralized manufacturing, it may have patient related benefits (logistical such as product availability or economic) even for current traditionally manufactured medicines.

### **Question 1:**

Do you agree that point of care manufacturing is sufficiently different to the current 'standard model' of factory-based manufacture of medicinal products that a new framework is required?

If no, please provide further information on alternative regulatory arrangements to cover POC products.

If yes, please provide further information on changes or additional arrangements that you consider to be required in order to support development of POC products.

### **ISPE Response to Question 1:**

Yes, ISPE agrees that POC manufacturing is sufficiently different to require a new regulatory framework, for the reasons discussed in MHRA's proposal. We have no additional considerations to add to the proposal in order to support development of POC products.

### **Question 2:**

Do you agree with the proposals for the new regulatory regime for POC products?

If no, please provide further information on alternative proposals to cover POC products.

If yes, please provide further information on changes or additional arrangements that you consider to be required. For the POC master file system, please include details on contents you consider appropriate.

### **ISPE Response to Question 2:**

Yes, in general ISPE agrees with the proposals, including the use of Master File Systems and the hub-and-spoke model. The concept of the control site and control site master file will allow flexibility to add new sites and manage QP release, but also account for appropriate documentation to ensure the quality, safety, and efficacy of medicines. However, ISPE recommends that the new framework is not limited in scope “to medicines that need to be manufactured and supplied in close proximity to patients or new supply chains that enhance patient access.”

### **Question 3:**

We are seeking to clarify the scope of the new POC regulatory framework in relation to the above manufacturing categories.

### **Question 3a:**

Do you consider that the new POC regulatory framework should be further adapted to also cover modular manufacturing?

### **ISPE Response to 3a:**

Yes, the POC regulatory framework should also cover modular manufacturing. There are at least three scenarios where modular manufacturing could greatly benefit from the proposed framework:

- 1) Networks of similar modular manufacturing facilities – these networks may develop out of need for local manufacture due to governmental desire for a local supply chain to provide more assured patient access or due to product nature. These networks may face similar challenges to those of POC.
- 2) Modular manufacturing that requires speed in implementation or other patient benefits – an attractive benefit of modular manufacturing is the potential speed of implementation – whether installation of a new site, or movement of a pre-existing site to the needed location. However, the conventional regulatory framework can lead to delays in implementation (full revalidation, inspections, etc.) despite the risk to product quality being less than a traditional manufacturing site move.
- 3) Modular manufacturing that does not have a planned receiving facility – An autonomous mobile, modular facility (e.g. on a truck trailer, or a caravan) may manufacture small amounts of a product to be delivered locally, and then moved to a new location with frequency.

As mentioned in the proposal, there may be overlap between the categories, and it makes sense then that the regulatory framework would also be amenable to overlap (i.e., application of current framework, or application of a control site and control site master file and allowances for QP and inspections).

### **Question 3b:**

Do you consider that the new POC regulatory framework should extend to cover home based manufacturing?

### **ISPE Response to Question 3b:**

ISPE has concerns over implementation of POC regulatory framework to home based manufacturing currently. There is a significant difference in capability between a trained manufacturing technician or health care provider, and average citizen; additional variables that have impact to product quality may be unknown and differ from manufacture by a trained individual. It may be necessary to implement additional controls for a home-based scenario. However, a time when manufacturing technology is simple and robust enough for home-use could be envisioned. For that reason, it would be useful allow for future home-based manufacturing in the legislation with considerations for additional controls to be defined later.

#### **Question 3c:**

Do you consider that there are other areas of POC manufacture that should be covered?

#### **ISPE Response to Question 3c:**

It would be useful to keep the scope of the legislation broad enough to ensure application for future scenarios that have not been currently considered to enable flexible/distributed manufacture.

#### **Question 3d:**

If you consider that this new framework should not be adapted to cover one or more of these above manufacturing categories, what regulatory controls do you consider are required?

#### **ISPE Response to Question 3d:**

Home-based manufacturing may require greater validation of manufacturing process reliability, as well as comprehensive studies to demonstrate home-based users are able to operate the equipment and follow procedures.

#### **Question 4:**

Are there other aspects of the POC framework that you believe have not been considered? This could include any additional positive and negative impact that the framework may have on the delivery of healthcare in the UK.

Please provide further information.

#### **ISPE Response to Question 4:**

It would be helpful to write the scope of the framework in an inclusive manner so that legislation might be applied in various circumstances that need or could benefit from the use of a control site concept as proposed.