20.12.2016

Submission of comments on **Concept paper on Good Manufacturing Practice and Marketing Authorisation Holders** (EMA/582064/2016)

Comments from:

| Name of organisation or individual |
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*Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.*

*When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).*

1. General comments

| Stakeholder number*(To be completed by the Agency)* | General comment (if any) | Outcome (if applicable)*(To be completed by the Agency)* |
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|  | **EFPIA supports the proposal to create a Reflection Paper** to capture all of the responsibilities that apply to Marketing Authorisation Holders (MAHs) to enable manufacturers to comply with GMP and clarify the relationship between MAHs and manufacturers. There are a number of key considerations which EFPIA would like to highlight for consultation with interested parties prior to publication of the Refection Paper:* Roles & responsibilities of impacted individuals
* Oversight of specific elements of Product Quality Review
* ICH Q12 and relationship between Inspectors and Assessors
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|  | **EFPIA requests the opportunity to review the draft Reflection Paper ahead of its finalisation**. It is recognised that the Reflection Paper will not introduce new requirements, however the clarification of some of the existing interpretations may introduce some queries, which would be best resolved prior to publication of the final document. |  |
|  | **Detailed comments:** |  |
|  | **Clarification of the responsibilities of the various pharmaceutical players within the Reflection Paper would be particularly helpful**, e.g. roles of Qualified Persons (QPs) in manufacturing sites, QPs overseeing importation activities, Responsible Persons listed on Wholesalers Licences (WDAs), MAHs, etc.. It is particularly important to clarify the requirements where the MAH and manufacturing site are part of the same global organisation and share a Quality Management System but may be different legal entities.  |  |
|  | **The illustrative examples included in section 2 of the Concept Paper are very useful** to exemplify the value of a new Reflection Paper. EFPIA considers that an exhaustive list in the Reflection Paper of all of the references to GMP for MAHs peppered throughout the EU Guide to GMP is essential; the mechanism for keeping this list current should be articulated within the Reflection Paper. |  |
|  | **EFPIA would like to further explore the direction of travel that some EU agencies are taking regarding periodic Product Quality Reviews (PQRs).**  We would like to take the opportunity created by the preparation of this Reflection Paper to further discuss and agree practical interpretations that ensure appropriate visibility of product quality data with minimal duplication of effort between manufacturing sites, the QPs at these sites, Regulatory functions and the various legal entities that constitute the ‘Marketing Authorisation Holder’ in order to find the best format for joint Product Quality Reviews between all parties. For example, Chapter 1 requires a Product Quality Review (PQR) to take into account the ‘qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc.’ which is an aspect of the PQR which the MAH would not typically be equipped to assess. Conversely, the review of ‘Marketing Authorisation variations submitted, granted or refused’ is a key element of PQR which MAHs should be responsible for reviewing. Consistent interpretation across the EU of accountability of all parties involved in PQRs would be welcomed. |  |
|  | **It is noted that amongst the areas that are not considered to be well addressed at present are the provision of the necessary registered details, the management of MA variations, and regulatory commitments to manufacturing sites.** Given the work currently being undertaken on ICH Q12 and the expectation that this will result in greater flexibility in post-approval lifecycle change management, it might be appropriate to include specialists undertaking EMA MAA assessments in the drafting group as well as GMP inspectors. |  |
|  | Building upon the point above regarding Q12, and the increasing global collaboration amongst agencies on GMP (with e.g. the EU/US Mutual Recognition Agreement in progress) triggers the need for a robust and transparent EU inspection process with clear roles & responsibilities for all parties due to the major impact decisions on GMP status can have on global supply chains. Thus, the scope of the Reflection Paper should be expanded to include consideration of how the MAH can interact with the supervisory GMP authority inspecting the manufacturing site, specifically in the case of critical findings which might trigger a change in the GMP status of the supplying site. Decisions impacting on the supply should only be taken following discussion between the GMP inspectorate and the National Competent Authority or EMA. This should include an appropriate "appeal" forum with a potential oral explanation by the applicant/MAH to provide further rationale.  |  |
|  | EFPIA supports the Reflection Paper being located within EudraLex Volume 4, Part III (GMP related documents). |  |
|  | Perhaps in the interest of clarity, the paper could be titled ‘The Interaction between Manufacturers and Marketing Authorisation Holders in the context of Good Manufacturing Practice.’ |  |