31 March 2015

Submission of comments on 'Concept paper on annex 1 of the guidelines on good manufacturing practice – manufacture of sterile medicinal products’ – CHMP/INS/GMP/735037/2014

Comments from: EFPIA

| 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)* |
| --- | --- | --- |
|  | EFPIA welcomes and supports the proposals to update Annex 1, although the sentence “*It is stressed that this is a clarification of current practices and that no new expectations will be created*” may imply that no changes to current requirements which, in EFPIA’s view, are in some cases needed in order to improve the annex. Scope EFPIA believes that the updated annex 1 will be less ambiguous if the scope of the remains very clearly focussed on the requirements to make sterile products, and that it should not confuse the requirements of upstream non-sterile processes such as aspects of biotech processing or vaccine intermediates which have been sometimes wrongly subjected to inspection per Annex 1 although they are not manufactured as “sterile” products.  The requirements for these non-sterile upstream processes should be considered in other more appropriate regulatory annexes (e.g. Annex 2 - MANUFACTURE OF BIOLOGICAL MEDICINAL PRODUCTS FOR HUMAN USE) Improved Clarity EFPIA supports any improvements to clarify and remove ambiguity of existing requirements; However it is also very important that the correct balance between clarity and over prescription is struck which will provide workable clear compliance requirements. For example:   * Holding times and their verification * Air velocity requirements (filter face vs working height) * Environmental monitoring frequency for different areas * Media fill requirements for campaigning  New Technologies EFPIA agree that the new annex should take into account the introduction of new technologies, for example   * Preparation of water: Use of Reverse Osmosis * Further guidance on the use of Restricted Access Barrier Systems (RABS). * Increase scope to include new microbiological testing technologies, e.g. real-time detection of viable particulates. * General guidance and new sections on technology such as microsphere and nanoparticulate suspensions.  Quality Risk Management Principles EFPIA member companies agree that there are aspects of annex 1 that will be improved with the inclusion of the principles of ICH Q9 (Quality Risk Management), and so it is important that the changes embrace risk management principles to eliminate arbitrary historical approaches, and instead rely on scientific rationale. ,For example:-   * Repetition of filter integrity tests (risk versus benefit of doing so both prior to use and after use) * Periodic sterilization/sanitisation of hot water systems * Rotation of disinfectants (clarify expectations and rationale)  Inclusion of Non-Sterile Aspects EFPIA generally supports the proposal to clarify Annex 1 with additional information on the requirements for the manufacture of non-sterile medicinal products. This revision is an opportunity to clarify some of these requirements, for example regarding vaccine intermediates such as polysaccharides which have been subjected to inspection per Annex 1, although they are not manufactured as “sterile” products. Harmonisation The revision of annex 1 provides an opportunity to address the standardisation with international guidelines such as the clean room classifications in draft ISO standard EN ISO 14644-1 and the harmonisation of terminology for example Laminar airflow replaced with unidirectional airflow. Question and Answer Document Following other excellent recent examples, the use of an extensive Q&A document aligned to the new annex may also be useful in giving additional clarity to the revised annex 1 |  |

1. Specific comments on text

| Line number(s) of the relevant text  *(e.g. Lines 20-23)* | Stakeholder number  *(To be completed by the Agency)* | Comment and rationale; proposed changes  *(If changes to the wording are suggested, they should be highlighted using ‘track changes’)* | Outcome  *(To be completed by the Agency)* |
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