Mr Andrzej Rys

European Commission
Directorate B: Health systems, medical products & innovation

B232 08/135, Rue Breydel 4,
1049 Brussels

Subject: Second targeted consultation on the GMP Annex 1

20 July, 2020

Dear Mr Rys,

The European Compliance Academy (ECA) appreciated the opportunity to review the 2nd draft of the revised Annex 1. ECA's Annex-1-Task-Force included members from companies with international reputation for producing small and large volume parenteral products, applying terminal sterilisation and / or aseptic techniques and aseptically manufactured sterile APIs.

Whilst the Task-Force is happy to confirmed that the 2nd draft is much clearer than the 1st consultation document, they would like to see further clarification of the text to ensure harmonised application of the requirements. Following EMA's request to focus on relevant comments, we have restricted the number of comments as summarized in the attached document.

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To keep regulatory requirements aligned, we ask the commission to consider harmonization with the recently implemented EMA guidelines; for example:

- *regulations in 4.1.4.2 Ethylene oxide sterilisation for empty containers in the "Guide-line on the sterilisation of the medicinal product, active substance, excipient and primary container", 6 March 2019, EMA/CHMP/CVMP/QWP/850374/2015*
- *regulations in 4.3.2. Aseptic environment for cleanroom classification in the "Guide-lines on Good Manufacturing Practice for Advanced Therapy Medicinal Products"*

In addition to our specific comments, the Task-Force also have a serious and overarching concern, which we would like to explain:

From consultation with regulatory stakeholders, who were involved in the revision of Annex 1, our understanding was that some manufacturers needed more detailed and precise guidelines on the requirements. We therefore anticipated the new version of Annex 1 to have more details in some areas, covering almost every eventuality.

However, using specific and or new technologies, entails conditions, under which QRM must be applied as it would be inadequate or even technically impossible to follow customary and standard approaches described in detail in Annex 1.

Our concern is that enforcing the implementation of these particular details may be preferred option for the inspectors, eliminating the acceptability of the company's

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adequate and/or QRM-based solutions for sophisticated and new technologies. Such an approach may prevent the application of QRM rather than encouraging it.

We restricted our comments on the meaningful and thoughtful implementation of QRM, trusting this will be acknowledged and accepted during inspections.

As a conclusion, we strongly suggest to avoid inadequately narrow interpretation, the implementation of the revised Annex 1 should be supported with QRM as the general **guiding** principle, not only by the practitioners in the industry, but also by the regulatory stakeholders.

Best regards,

Dr Afshin Hosseiny
Chairman of the ECA Foundation

Dr Ulrich Kissel
Chairman of the European QP Association

Dr Ingrid Walther
Lead of the Annex 1 Task Force

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