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**Submission of comments on the Consultation Document**

**'GOOD MANUFACTURING PRACTICE FOR ADVANCED THERAPY MEDICINAL PRODUCTS'**

Comments from

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**EUCOPE RESPONSE TO THE CONSULTATION DOCUMENT 'GOOD MANUFACTURING PRACTICE FOR ADVANCED THERAPY MEDICINAL PRODUCTS'**

**Introduction**

This response to the European Commission, Unit B5 – "Medicinal products – policy, authorisation and monitoring" consultation on the ‘Good Manufacturing Practice for Advanced Therapy Medicinal Products’ document is submitted by the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) on behalf of its member company Miltenyi Biotec GmbH.

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| **Line number of the relevant text in the consultation document** | **EUCOPE comments and proposed amendments** |
| General: | Comment:  EUCOPE on behalf of its member company Miltenyi Biotec highly welcomes the proposals made in the consultation guidelines paving the way for feasible ATMP development in Europe and leading to increased availability of these product without making compromise to quality and safety of the products. |
| 128-130 | Comment:  It should be clarified that current other guidelines (e.g. EU-GMP) will no longer apply to ATMPs or at least have to be considered together with GMP for ATMP Document.  Amendment proposal:  We strongly recommend cross-referencing to this consultation document where applicable. |
| 151 f.  *“…and allogenic products in a donor matched scenario:”* | Comment:  Allogenic products are not always donor matched. Hence this should also apply to HLA-mismatched settings, which is a common clinical situation or not applicable in certain settings or for certain products. |
| 461-471 | Comment:  For clarification please add that each closed system is to be regarded as an area (as referred to in line 1268). |
| 461-462 | Comment:  It should be clarified that if ATMPs and non-AMTPs are manufactured in separate closed systems, then they can be manufactured in the same facility (see comment to line 461 above) because closed system should be considered as physical segregation |
| 462 | Comment:  It should be clarified that if ATMPs and non-AMTPs are manufactured in separate closed systems, then they can be manufactured in the same facility (see comment to line 461 above) because closed system should be considered as physical segregation. |
| 481-483 | Comment:  It should be clarified that „contaminated materials“ means e.g. patient material or waste material (definition of “contaminated materials”). |
| 506-507 | Comment:  This statement is supported strongly. |
| 516-519 | Comment:  contradiction to line 322 |
| 659 f.  *„The location and installation of the equipment should be adequate to minimize risks of errors or contamination. Aseptic connections should be performed in a critical clean area of grade A with a background clean area of grade B.“* | Comment:  For first in man trials it is accepted to make connections in an A in C area  (line 322 f.), which contradicts the statement above.  Amendment proposal:  We suggest to add the same sentence to the statement in lines 659 f. as well in order to harmonize the requirements. |
| 660-661 | Comment:  Aseptic connections can also be done by sterile tube welding (functionally closed systems) which do not need a grade A in B. Current wording is too categorical.  Amendment proposal:  We suggest to add the following sentence: Aseptic connections can also be made using a functionally closed system such as sterile tube welding. |
| 1227-1229 and f. | Comment:  We would like to propose additional definitions with regard to aseptic connections (e.g. needles in septum, luer locks), sterile connections (e.g. tube to tube welding, aseptic connections with a sterile septum and spikes with filters). |
| 1268 f. | Comment:  We would like to clarify that the term „closed system“ still applies in case of spiking of buffers is an aseptic process if the buffer is sterile filtered before reaching the closed system by the use of micro-organism retentive filters. |
| 1270 | Comment:  The meaning the “exhaust air of isolators/closed systems with separated expulsion” is not clear.  Amendment proposal:  We suggest that exhaust air filtration is appropriate. |
| 1624 | Comment:  Validation of the manufacturing process for investigational ATMP is not necessary. Contradictory to the requirements to get a manufacturing license where validation is necessary in general. |
| 1808 | Comment:  Could the regulators please give advice on how the QP is responsible: are those kind of “out-of-spec products” obliged QP-release before administration or are the doctors solely responsible and no QP-release is needed?  Amendment proposal:  if physician wants to administer, the product has always to be QP-released. A strong QP-Doctor-interaction is needed to assess the risk/impact of the specific OOS-result. |
| 1816-1817 | Comment:  This requires an established system by the authorities so more clarification on notification process is needed. |
| 2081 | Comment:  What is a substantial manipulation? Regulation (EC) 1394/2007 Annex 1 defines only non-substantial manipulations. At least there should be a cross-reference to Regulation (EC) 1394/2007 regarding manipulation definitions. |
| 2176 f.  *“controlled but non-classified background environment acceptable for short processes (while patient waiting)”* | Comment:  This paragraph doesn’t consider longer procedures while patient might be even waiting at home - why limit to short processes while patient is in surgery? A validated closed system is proven for having no contact between the product and the environment, even reduced particle monitoring is acceptable if justified (refer to lines 572 f.), so if the patient can wait days during manufacture, so longer procedures performed under validated closed system should also be manufacturer controlled non classified room for weeks. |
| 2200 (end of the line) | Comment:  number of the section to refer to is missing. |
| 2202-2203 | Comment:  Same QP can be responsible for more than one site for the release of the product. Need more precision: is there still the need of a QP per manufacturing site? Can the “central” release of the multi-site-QP take place on its own or the local release by the local QP needed first? |