STEMCELL™ TECHNOLOGIES

10 November 2015

Unit D5 "Medicinal products – Authorisations, European Medicines Agency"
SANTE-D5-ADVANCED-THERAPIES@ec.europa.eu
European Commission
DM24 02/133
B-1049 Brussels (Belgium)

**re: Targeted stakeholder consultation on the development of Good Manufacturing Practice for Advanced Therapy Medicinal Products pursuant to Article 5 of Regulation 1394/2007**

To the Directorate General for Health and Food Safety,

Thank you for the opportunity to provide comments on the consultation Document "Good Manufacturing Practice for Advanced Therapy Medicinal Products", on behalf of STEMCELL Technologies Inc.

STEMCELL is a leading Canadian supplier of raw materials to the cell therapy industry. As a rapidly growing company, it exceeds the EU definition of a small or medium-sized enterprise. STEMCELL is not registered in the Transparency Register.

Our collected comments are attached.

Best regards,

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cc: Ian Rees, MHRA

**Comments**
**Consultation Document: Good Manufacturing Practice for Advanced Therapy Medicinal Products**
**Published for Targeted Stakeholder Consultation from 23 July, 2015 to 12 November, 2015**


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| Section | Line Number(s) | Questions | Comment and Rationale |
|---|---|---|---|
| 2. GMPs for ATMPs: general principles | 75 | Q2: Do you consider it useful that additional level of detail regarding the application of the risk-based approach is provided in the Guideline? In the affirmative, please provide examples. | Yes. It is critical that Sponsors understand the value of implementing a phased / risk based approach to Quality. The most critical consideration patient safety, which must always remain at the forefront of a risk-based approach. But consideration to the business risk is also important to ensure continued innovative contribution occurs in the market. For example, a very high percentage of Phase I clinical trials fail; as such, is it wise to apply commercial-scale quality requirements to early phase clinical trials? If we do that, companies will likely run out of money before they can contribute to furthering the market – again, never losing sight of patient safety.<br><br>You have eloquently captured this thinking in lines 120-122. “While an acceptable level of quality must be ensured for investigational ATMPs, it is acknowledged that additional flexibility is warranted, in particular for early phases of clinical trials.” |

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|---|---|---|---|
| | | Q3: How should the quality systems established in accordance with Directive 2004/232 be recognised in terms of GMP compliance for products that are ATMPs solely because the use of the relevant cells/tissues is for a different essential function in the recipient as in the donor (i.e. the manufacturing process does not involve any substantial manipulation)? What about the JACIE accreditation system? | There should be alignment of GMP concepts / requirements, keeping patient safety as the paramount consideration. |
| 4.2.1 Design and construction | 202 | "The laid out of the premises…" | Replace with "The lay out of the premises…" |
| 4.2.2 Aseptic environment | 214-215 | "For commercial production of ATMPs, the premises should be fully validated." | Please clarify whether production of clinical ATMPs would also require full validation of the premises. E.g. Do premises need to be fully validated for Phase I? |
| 7. Starting and raw materials | 442-514 | Are the requirements laid down in Section 7 sufficiently well adapted to the specific characteristics of ATMPs? | There is no real delineation in this entire section between raw materials and starting materials. Areas of this section interchange both terms freely making it confusing to understand what requirements apply to which type of material. Recommend adding distinct definitions and requirements for each to clarify qualification strategies using a risk based approach. |
| 11.3.1 Batch release process | 799-801 | "The process of batch release includes the following steps:<br>The source and specifications of starting materials and packaging materials comply with the terms of the market authorization or clinical authorization, and the provisions in Section 7 and 9.5.," | Recommend adding raw material requirements to this section. |
| 12.2 Sampling | 928 | "Sampling of primary packaging and critical raw materials should be kept." | Please clarify the recommendation for non-critical raw materials. |
| 12.3 Testing | 954 | "Identity testing of starting materials…" | Please clarify if identity testing of raw materials is also required. |