European Medicines Agency

**SUBMISSION OF COMMENTS ON**

**PROPOSALS TO AMEND ANNEX 1 TO DIRECTIVE 2001/83/EC, AS REGARDS ADVANCED THERAPY MEDICINAL PRODUCT REGULATION**

**Version: 8 April 2008**

**COMMENTS FROM: Pfizer**

**GENERAL COMMENTS**

Pfizer welcomes the opportunity to comment on the Public Consultation Paper concerning the proposed amendments to Annex 1 of Dir 2001/83/EC, to include Advanced Therapy Medicinal Products, to replace the existing Part IV of this Annex and facilitate a harmonised approach to the regulation of these products across the EU.

Pfizer considers the document to be well-written, comprehensive and concise in accommodating ATMPs. However, some of the points made regarding starting materials may be unnecessarily duplicated as they are captured in the requirements for biological/biotechnology products. We have made some more specific suggestions on the text below.

It would be useful to include a list of the relevant guidance documents pertaining to ATMPs, including those in draft or being proposed by EMEA.

It should be acknowledged that these innovative products will require the development of new tools and techniques to establish the safety and efficacy and comply with emerging regulatory requirements.

**SPECIFIC COMMENTS ON TEXT**

| Page no. + paragraph no. | Comment and Rationale | Proposed change (if applicable) |
|---|---|---|
| **Pg 2 section 2.2.1** | | |
| | Definition of a GT product | Would it be possible to clarify/confirm if synthetic oligonucleotides/ ribonucleotides are within scope of the GT definition or not or will this be set out in a separate guidance? |

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|---|---|---|
| **Page 6; Section 2.3.2** | | |
| **Point 1, first bullet** | Missing word? | Insert the word “packaging” after “the master cell bank of the *packaging* cell line” |
| **Point 3** | Suggest text amending to read “the general requirements for medicinal *and biological/biotechnological* product *shall* apply” | |
| **Point 5** | Possible ambiguity. | Suggest inclusion of s sentence to the effect that “The principles of GMP shall, were relevant, apply to the generation of the host cell bank system onwards” |
| **Point 5 b** | Suggest inclusion of the following: | “data on the genetic *sequence and any* modifications” |
| **Point 5 f** | Suggest inclusion of the following: | “For genetically modified cells the *required or intended* phenotypic…” |
| **Page 7Section 2.3.3** | | |
| Point 1 | Clarification is required as to why this point specifically applies to SCT and TEPs? | |
| Point 2 | Please clarify for this type of product if pre-clinical testing is required for the active substance (cells), excipients and additional substance e.g. scaffolds and matrices separately and/or in combination (final product) only | |
| Point 6, a, i | Please define what is meant by “non-healthy cells” | |
| Point 6,a,iii | Consider inclusion of adventitious agents here also. | |
| Point 6, b, iii | Validation may be difficult to define for some SCT and TEPs. The development of appropriate guidance for this type of product would be helpful. | |
| Point 6, c | Much of this is applicable to other types of GT and biological/biotechnological products; is this duplication required here? | |
| Point 6, e | Suggest amending wording as follows: | The description of the development program should *summarise and justify* the choice of materials and processes. |
| Point 6, f | This could be problematic for some types of SCT or TEP and the development of EU guidance on appropriate reference standards for this type of product would be helpful. | |

| Page 12 & 13Section 2.4.2 | | |
|---|---|---|
| Point 1 Pharmacology | Guidance is required as to the scope of the studies that will be required for SCT & TEPs. Sponsors may wish to test the final product in an animal model before proceeding to patients. Animal models may suffer from a lack of cross-reactivity and therefore relevance of pharmacological data. Larger animal studies may require immunosuppression which may complicate data interpretation. | |
| Point 2, b | Further clarification is requested on this point. Is the expectations for sponsors to develop autologous models (mouse cell is mice with mice secreted proteins – if homologous to the human protein)? Cross reactivity issues may generate PK but not PD data. | |
| Point 3 Toxicology | Further guidance is requested to clarify the data requirements for toxicology studies on SCT and TEP to include suggestions on study duration, species selection and design. | |
| Point 3, g, second paragraph | Suggest inclusion of the words “were relevant” at the end of this sentence as it may prove problematic to generate relevant pharmacological/immunological data in an animal model. | |