Comments for Consultation Document:
Good Manufacturing Practice for Advanced Therapy Medicinal Products
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Line number(s) of the relevant text	General comment (if any)
Different sections- general comments	It is suggested to include attention to xenogeneic ATMPs in the document. There is experience at EMA with xenogeneic cell therapy products that are classified as ATMP. In line with this, EMA has issued a ***Guideline on xenogeneic cell-based medicinal products*** **(EMEA/CHMP/CPWP/83508/2009)** which could be referenced.
Different sections- general comments	In various sections of the document storage periods are mentioned, which are variable (e.g. section 6.5, line 426-441; section 11.3, lines 834 n 839; section 12.2, lines 939). This might cause some confusion, since in Regulation EC1394/2007 there is only one place where storage is mentioned, namely in Article 15, Traceability, paragraphs 1 and 4: *1. The holder of a marketing authorisation for an advanced therapy medicinal product shall establish and maintain a system ensuring that the individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the hospital, institution or private practice where the product is used.* *4. The marketing authorisation holder shall keep the data referred to in paragraph 1 for a minimum of 30 years after the expiry date of the product, or longer if required by the Commission as a term of the marketing authorisation.* This 30-year storage period is also mentioned for records in the EMA Guideline on xenogeneic cell-based medicinal products mentioned above. Is is proposed to include in the document a table summarizing the storage periods for various items (samples, records, etc) mentioning also its application to various phases in development and after market authorisation.
Line 489-492	This regards the paragraph on antibiotics. It is proposed to give attention to the animal source of a

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	xenotransplantation product. The above-mentioned EMA Guideline on xenogeneic cell-based medicinal products is clear in this respect, see the section on Veterinary control (section 2 in 4.2.1. Starting and Raw Materials): *Protocols for monitoring the herd for disease and infectious agents should exist. Specific screening procedures should include appropriate physical examination and laboratory tests. All infectious agents known to potentially infect the source species have to be considered including viruses, bacteria, mycoplasma, fungi, TSEs and parasites. The herd health surveillance system should include comprehensive documentation of all veterinary care received. The use of antibiotics and vaccination of source animals is not recommended. If the treatment of animals with any medicines is necessary for animal welfare reasons, an evaluation of the impact on the product should be performed, and discussed with the competent authority. Any use of vaccines must be justified.* Reference is also given to the FDA's ***Guidance for industry: source animal, product, preclinical, and clinical issues concerning the use of xenotransplantation products in humans*** (http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Xenotransplantation/ucm074354.htm), mentioning the documentation of antimicrobial agents in Chapter 2, section c, Health Care: T*he herd health surveillance system should include comprehensive documentation of all veterinary care received by source animals. This includes documentation of all illnesses, medical care, procedures, drugs administered, vaccinations, routine physical exams, and any treatments received by each animal. You should carefully document use of antimicrobial agents due to potential risk to allergic recipients receiving unprocessed nonhuman live cells, tissues or organs. You should validate residual drug levels to be insignificant in cells, tissues, or organs taken from source animals that previously have received medications. Exclusive use of killed vaccines generally is warranted both in the source animal and in the herd with which it is associated. You should use live vaccinations only when alternative immunogens for vaccinations are not available, and only if scientific evidence exists to support that the live cells, tissues, or organs from the vaccine-treated animal will not pose a risk of infection for the human recipient.*
Line 648	This regards the statement on cleaning validation. It is proposed to open the possibility that validation is required after market authorisation, and that the developmental period during clinical rials is used for cleaning verification. Especially when production cannot be done in a campaign-approach (particularly cell therapy products) the requirement for cleaning validation might raise problems in the clinical development phase.