Annex I to Directive 2001/83/EC – comments

1) The starting materials for gene therapy medicinal products are mentioned twice in the document. First, they are described in paragraph 2.3.2., points 1 and 2. For the second time, they are listed in point 5(a) of the same paragraph. Most of the provided information is repeated (using different wording) in the abovementioned paragraphs. These points should be combined together and the information about starting materials should be deleted from points 1 and 2. Point 5(a) is more detailed and more comprehensible.

2) The requirements for the use of genes for antibiotics resistance should be mentioned in point 5 of par. 2.3.2. There are many questions concerning the usage of these genes with regards to safety of gene therapy drug products, so this point should be highlighted in the document. The proposed wording is: The use of genes for antibiotics resistance should be avoided in gene therapy medicinal products whenever possible. If these genes are used, their use should be justified with regards to the safety of the medicinal product.

3) 2.2.1.: Rewording of the gene therapy medicinal product's definition is proposed because the term *in vivo* or *ex vivo* is not related to the way of use or administration of the medicinal product, but only to the strategy of the manufacturing process:
Gene therapy medicinal product
means a medicinal product:
that contains or consists of a nucleic acid sequence used in or administered to human beings, **using** *in vivo* or *ex vivo* **strategy**, with a view to regulating, repairing or replacing a targeted genetic sequence; and
whose therapeutic, prophylactic or diagnostic effect relates directly to the nucleic acid sequence it contains, or to the product of genetic expression of this sequence.

4) 2.2.2.: The definition of the somatic cell therapy medicinal product should include information about the origin of cells and specify whether the cells may be viable or non-viable. In case of a tissue engineered product, this information is included in Article 2 (1) (b) of Regulation 1394/2007/EC. Viability and origin of cells or tissues that are contained in a somatic cell therapy medicinal product are basic parameters that should be mentioned in the definition.

5) 2.3.2.-2.: It is stated that genetically modified cells may be grown on or within a medical device, but the medical device may have other functions as well. The sentence should be reworded as follows: In some cases, the finished medicinal product may be ~~grown on or within~~ **combined with** a medical device.

6) 2.3.3.-6.(c)(i): Genetic stability of the cells shall be ~~described~~ **demonstrated**.