Merck Serono COMMENTS ON Advanced Therapies Regulation 1394/2007 –

Public Consultation Paper: Proposal to amend annex I to Directive 2001/83/EC as regards advanced therapy medicinal products

DETAILED COMMENTS

Section	Comments
Section 2.1 Introduction	We would welcome a clarification, that the document does not apply to new drug products and new drug substances during the clinical research stages of development.
	From our point of view in general chemically synthesized products should be excluded from the scope of the document. For the reasons listed below we would propose to include a explicit statement that the document does not apply to chemically synthesized products as antisense oligonucleotides etc.
	Risk analysis as described is also not applicable to chemically synthesized products.
Section 2.2.1	From our point of view chemically synthesized products e.g. oligonucleotides, which are currently covered by the definition given in section 2.2.1, should be excluded from the scope of the guideline.
	This is suggested based on several reasons: The quality part of this document does not cover synthetically-derived gene therapy medicinal products adequately which are completely different with regard to quality requirements in comparison to biotechnologically-derived products. For example, completely different ways of synthesis for NCEs (e.g. oligonucleotides) are used and, therefore, different requirements have to be applied. The whole document refers mainly to biotechnologically-derived products. As the document currently applies per definition in general to gene therapy medicinal products, whose therapeutic effect relates directly to the nucleic acid sequence it contains, e.g. chemically synthesized oligonucleotides would also be covered.
Section 2.3.2 Bullet point 3.	This statement concerning quality data is not clear. It is stated that “For gene therapy medicinal products, the general requirements for medicinal products apply” – but e.g. chemically synthesized oligonucleotides (NCEs) are explicitly excluded from ICH Q3A and ICH Q3B, ICH Q6A so there is currently no specific guidance. If this sentence is related to GMP requirements this should be clearly stated. Please clarify this point.
General	In general, there should be a differentiation between DNA- and RNA-based products. (e.g. with regard to the risk of integration into the genome, etc.) The different modes of action of advanced therapy medicinal products should be considered. Aptamers like antisense oligonucleotides have specific three-dimensional structures that can form complexes with target proteins and inhibit their activity. Unlike the other nucleotide-based strategies, complementarity is not important for the activity of aptamers; their tertiary and quaternary structures determine their binding.