SUBMISSION OF COMMENTS ON

PROPOSALS TO AMEND ANNEX I TO DIRECTIVE 2001/83/EC AS REGARDS ADVANCED THERAPY MEDICINAL PRODUCTS
Doc. Ref. EMEA/2001-83-EC/1394-2007

COMMENTS FROM Schering-Plough, Lisette Vromans
GENERAL COMMENTS

SPECIFIC COMMENTS ON TEXT		
GUIDELINE SECTION TITLE		
Line no[1]. + paragraph no.	**Comment and Rationale**	**Proposed change (if applicable)**
Page 14, 2.5.2 Specific requirements for gene therapy medicinal products 1. Human PK Studies - Shedding	The proposal asks that the following aspects of human pharmacokinetics be addressed: • shedding studies to address the excretion of the gene therapy medicinal products; We believe this section should be modified as shedding studies only make sense for gene therapy medicinal products that consist of a replication competent virus or vector.	Change to: 1. Human Pharmacokinetic (PK) Studies shall include the following aspects: • *For gene therapy medicinal products that consist of a replication competent virus or vector, shedding* ~~shedding~~ studies to address the excretion of the gene therapy medicinal *product* ~~products~~;
Page 14, 2.5.2 Specific requirements	The proposal asks that the following aspects of human pharmacokinetics be addressed:	Change to: 1. Human Pharmacokinetic (PK) Studies shall include the following

[1] Where available

for gene therapy medicinal products 1. Human PK Studies - Biodistribution	• biodistribution studies, including distribution to gonads; We believe this section should be modified as clinical studies do not readily lend themselves to invasive sampling needed for biodistribution studies. For example, biodistribution studies may need to be limited to sampling of blood, urine and other excreta such as semen. Gonadal distribution requirements for human studies should be based on nonclinical findings and should follow the recommendations in ICH Considerations: General Principles to Address the Risk of Inadvertent Germline Integration of Gene Therapy Vectors (October 2006).	aspects: • *biodistribution studies, limited to blood, biopsies, and if necessary - excreta or semen ~~including distribution to gonads~~;* • *gonadal distribution studies shall be conducted unless the lack of these studies is scientifically justified, e.g. because nucleic acid sequences will not enter into the cell nucleus, and no evidence for the need was found in nonclinical studies;*

Please feel free to add more rows if needed.