SUBMISSION OF COMMENTS ON:

Draft Amendments to the Clinical Trial Application Form as regards Advanced Therapy Medicinal Products

COMMENTS FROM: European Biopharmaceutical Enterprises (EBE) Contact person: Piers Allin (piers@ebe-biopharma.org)
GENERAL COMMENTS
Over all the updates in reference to ATMP in CTA application form are considered very useful. We recommend certain changes in positions of various sections in the updated application form. Additionally, we recommend to add in some additional information in reference to First in Human guidelines i.e. mode of action, nature of the target & relevance of animal models.

COMMENTS ON TEXT

Precise Reference and page of consultation document	**Comment and Rationale**	**Proposed change**
Pg 8/11 Section D3.11 to D3.11.4 and D4	Is it expected that at the start of the first clinical trial the sponsor will know the classification of the future ATMP. The regulatory classification of these products, borderline products and subclasses of ATMPs is complex. The definitions in the legislation are broadly based and confirming classification on a case-by-case basis through the CAT will take more than 60 days.	
Pg 8/20 Section D3.11 Type of IMP	The statement 'If yes to D.3.11.11' should be replaced by 'If yes to D.3.11.12' since additional questions related to contained use are related to GMM (genetically modified microorganisms) and not homeopathic products	Please update the section numbers in the statement: 'If yes to D.3.11.11' should be replaced by 'If yes to D.3.11.12'

Pg 8/20 Section D3.11 Type of IMP	Section D.3.11.10 Herbal Medicinal Product and D.3.11.11 Homeopathic medicinal products, position in the section D.3.11 Type of IMP will be more suited after the current section D.3.11.12 Products containing Genetically modified microorganisms.	Please update section numbers as follows: D3.11.10 Genetically modified microorganisms D3.11.10.1 D3.11.10.2 D3.11.11 Herbal Medicinal Products D3.11.12 Homeopathic Medicinal Products
Pg 8/20 Section D3.11 Type of IMP	Section D.3.11.13 is it an IMP to be used in first in human clinical trial, should appear after section D.3.11.14 Any other type of medicinal product. We consider that the first in human clinical trial information is also applicable for any other type of medicinal products as well.	Section D.3.11.13 Any other type of medicinal product. Section D.3.11.14 Is it an IMP to be used in first in human clinical trial
Pg 8/20 Section D3.11 Type of IMP & 312 Mode of action	Section D3.11.13 is it an IMP to be used in first in human clinical trial and its subsequent subsection D3.11.13.1 if yes, are there any risks identified according to FIH guidelines. It may be useful to introduce in this section the 3 potential risk factors as identified in the FIH guidance (i.e. particular lack of knowledge regarding the mode of action, nature of the target, relevance of animal models).	Propose, to add in section D3.11.13.1 three more sub-sections in reference to First in Human clinical trials guidance i.e. Mechanism of action, Nature of the target and Relevance of animal models.
Pg 9/20 D.4 Somatic cell therapy IMP	Section D4: Somatic cell therapy IMP (no genetic modification). Can be more explanatory if at the beginning of section we can add the text:	Section D4: * Somatic cell therapy IMP: yes/no * Genetic modification: yes/no; if yes, go to section D5.

	* Somatic cell therapy IMP: yes/no * Genetic modification: yes/no; if yes, to section D5.	
Pg 9/20 D.4 Somatic cell therapy IMP	D.4.2.3: Others? Which type of cells would fall in "others" category. It will be helpful to get clarification and few examples.	
Pg 10/20 D.5 Gene therapy IMP	Section D5.5.: Genetically modified **somatic** cells. It will be more explanatory if we can add in Genetically modified somatic cells.	Section D5.5.: Genetically modified **somatic** cells.
Pg 10/20 D.5 Gene therapy IMP	Section D5.5.4: Other type of cells (hematopoietic stem cells): This section can be elaborated to be more explanatory to provide information for different type of cells (see also section D4.2): * Type of cells: - Stem cells - Differentiated cells - if yes, specify the type (keratinocytes, fibroblasts..) - Others. - If others, specify:	Section D5.5.4: Type of cells: D5.5.4.1 - Stem cells D5.5.4.2 - Differentiated cells D5.5.4.2.1 - if yes, specify the type (keratinocytes, fibroblasts..etc) D5.5.4.3 - Others. D5.5.4.3.1 If others, specify:
Pg 10/20 D.6 Tissue engineered Products	Please clarify the statement 'The indication that determines that this is a tissue engineered product as opposed to a Cell Therapy product is given in section E.1.1'. Annex I of the Regulation of the EP & Council on Advanced Therapy Medicinal Product does not define the target indication under investigation as a criterion for distinction between tissue engineered products and somatic cell therapy products. Further guidance is required on this statement.	Please define.

Pg 14, section E7 trial type and phase	Please advice as we consider it to be useful to add in the paediatric studies here in trial types.	Please advice.