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The Directorate-General for Health and Consumers,

Unit SANCO/D/5,

BE-1049,

Brussels,

Belgium

18th December 2013

Dear Sir/Madam

RE: PCPIP/13/01 — Public consultation on PIP

The Cell Therapy Catapult is an independent, not-for-profit research organisation based in London, UK and core funded by the UK government's Technology Strategy Board. The Cell Therapy Catapult collaborates nationally in the UK and globally to take cell therapy products through the clinical development process and provides technical expertise and infrastructure to ensure cell therapy products can be made to the required quality standards and delivered cost effectively. This activity is expected to generate a strong UK cell therapy industry delivering health and wealth.

The Cell Therapy Catapult has been designated as an SME by the European Medicines Agency (Number: EMA/SME/083/13). Cell Therapy Catapult welcomes the opportunity to comment on this concept paper regarding the format and guidance for the submission of a paediatric investigation plan.

We detail below a number of points for which we seek further clarification and/or expansion.

1 General Comments

Cell Therapy Catapult would welcome more recognition of cell, gene and tissue therapies in the guidance document as many of the terms and notes refer to more conventional pharmaceuticals and medical devices and therefore may not be relevant to the development of these Advanced Therapy Medicinal Products (ATMPs).

Cell Therapy Catapult recognises that ATMPs represent a diverse class of therapies with different risk profiles and features and would welcome inclusion in the guidance of an acknowledgement that a case-by-case assessment for each therapy based on its individual characteristics is warranted.

2 Specific Comments

SECTION 2. FORMAT AND CONTENT OF APPLICATIONS FOR AGREEMENT ON OR MODIFICATION OF A PAEDIATRIC INVESTIGATION PLAN AND REQUESTS FOR WAIVERS AND DEFERRALS

2.2 Part A: Administrative and product information

2.2.8. Planned application for marketing authorisation/line extensions/variation

For medicinal products not yet authorised, which will fall under the requirements of Article 7 of the Paediatric Regulation, the date of completion of adult pharmacokinetic studies should be provided. When an application is submitted later than upon completion of the human pharmacokinetic studies in adults, a justification should be provided in this section.

Cell Therapy Catapult would like to draw attention to the fact that a number of ATMP products will not undergo traditional PK studies. Cell Therapy Catapult therefore suggest that alternative requirements are also stated for completeness.

2.3 Part B: Overall development of the medicinal product, including information on the conditions

2.3.3. Significant therapeutic benefit and/or fulfilment of therapeutic need

As experience with the use of the medicinal product in the paediatric population might not be available or might be very limited at the time of submission of the application, significant therapeutic benefit might also be based on well-justified and plausible assumptions. The application should explore these assumptions based on reasoned arguments and relevant literature.

The Cell Therapy Catapult considers this section to be particularly relevant for ATMPs / orphan medicines and therefore a reference to these types of products might be beneficial.

2.5 Part D: Paediatric investigation plan

2.5.2 Paediatric formulation development

For ATMPs, the final pharmaceutical form will often be derived from a cellular active substance that cannot be re-formulated for paediatric use due to the need for a highly specified delivery method and / or extracellular environment. Cell Therapy Catapult would like this to be acknowledged in this guidance document.

2.5.3 Non-clinical studies

Many ATMPs are being developed to treat diseases and conditions for which there is a lack of suitable animal models, making standard preclinical testing unfeasible or uninformative. Cell Therapy Catapult would like this to be acknowledged in this guidance document.

2.5.4 Paediatric clinical studies

SECTION 4. CRITERIA FOR ASSESSING THE SIGNIFICANCE OF STUDIES STARTED BEFORE AND COMPLETED AFTER THE ENTRY INTO FORCE OF THE PAEDIATRIC REGULATION

In the case of ATMPs, interventional trials involving innovative surgical techniques are very common and as a result, will require highly specified training and skills. The Cell Therapy Catapult suggest that the differences in surgical techniques and availability of paediatric surgeons who can perform the procedures should be considered.

4.2 Assessment criteria

In order to be considered as significant, the studies should normally cover several paediatric subsets affected by the condition where sufficient data are not available, unless a waiver has been granted. However, on a case-by-case basis, studies conducted in a single subset of the paediatric population could be considered as significant if sufficiently extensive or if they make

an important contribution to treatment of children or if they are carried out in a subset considered particularly difficult to study, for example neonates. Where sufficient data for one or more of the paediatric subsets are already available, duplication of studies should be avoided and therefore unnecessary studies will not be considered as significant.

Consultation item No 3: Do you have any comments on the assessment criteria for significant studies?

It may be difficult for ATMPs, many of which are developed for orphan and ultra-orphan indications, to fulfil this criteria. The Cell Therapy Catapult recognises that the guidance acknowledges that other studies could be considered significant on a case-by-case basis, however, we would welcome an expansion of the acknowledgement of acceptance of exceptions

Consultation item No 5: Please feel free to raise any other issues or make any comments which have not been addressed in the consultation items above.

Cell Therapy Catapult would encourage the addition of a section for ATMPs to this guidance document which would address the unique challenges to that product type and their use in the paediatric population e.g. the lack of suitable animal models, randomised trials with placebo product may not be ethically sound, early study in paediatrics may not be ethically acceptable, complex surgical procedures, sometimes very limited paediatric patient numbers and the requirement for long-term / lifelong follow-up etc.

We hope you find these comments helpful, please do not hesitate to contact me should you require any clarification on any of the points detailed in this document.

Yours sincerely

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