DRAFT AMENDMENT TO THE CLINICAL TRIAL APPLICATION FORM AS REGARDS ADVANCED THERAPY MEDICINAL PRODUCT.

Comments :
Add information inside the IMP to include characteristic and definition of advanced therapy product.

Tissue engineering product :
Description of the final product composition: need to be added: example : interaction between the device and cell, modification of characteristic of cell by the device for example.
Medium and package are the characteristic of the final product.
Description of cell
Description of the device
Description of the raw material ? if the medium, grow factors for the expansion is mandatory ?

NB : D9 : modified the note of the D9 report to the D8.2

DRAFT DETAILED GUIDELINE ON GOOD CLINICAL PRACTICE SPECIFIC TO ADVANCED THERAPY MEDICINAL PRODUCT.

I would like to point out that the stress coming from the writing of the long term follow up and the traceability for advanced therapy (no restriction) This could give difficulties to insure this trial and SME could have real difficulties to be sponsor of this kind of trial with the product. This comments is following the 2.2 article.
The insurance is asking before that the product had an evaluation by the national competent authority.. so no discussion and no evaluation..
But in an other hand, It seem that it is normal to have specific guidelines for advanced therapy, many cells are manipulated, but the follow up of the patient included in the trial need to be considered.
But maybe some consideration of innovative product (never implanted, or poor data) or data of similar product in other hand could be added in the IMPD and risk analysis or in the patient information.

No comment of the 2.3.1 and 2.3.2 about the responsibility.
Add that the Tissue Establishment: donor data follows the directives (Article 25, chapter V of the directive 2004/23); and final labeling of the 2006/86.

Adverse events or SUSAR:
Following the 2001/20 with the VIGILANCE
The alert could or need to be done to the manufacturer and the tissue establishment, by dependant the national authority Ex: Belgium donation establishment (multiorgan donation), France manufacturing (myocytes cells) Poland SAE.
Poland need to inform France and Belgium, because the impact of an organ transplant (Tissue establishment) could be relevant, or impact of other batch for the manufacturer could be relevant too. Some quick feedback to biovigilance needs to be organized in a schema. Do not forget maybe not in this guideline: the organization schema coming from the biovigilance to the sponsor…
(in the last example: problem to the donor to be reported to the sponsor..)

Protocol:
Characteristics of final product (combined or not specification of the medical device and range of cell…) need to be write in the IMPD, and the protocol describes the final product exactly, and has no vocation to explain separately parts of the product (cell with range modified.., performance of the device (different in the final combined product). The protocol need to give informations of critic raw materials : bovin serum, autologous serum , grow factors added for expansion..
Benefit/ Risk needs to be defined in the protocol, and in the patient information.
First paragraph: This example of characteristic of the product needs to be excluded in the protocol: It is IMP information's
I do not agree with the flexibility of protocol: inclusion or exclusion for example: criteria need to be maybe more strict.
Design of study could be different but not flexible.

Laurence Barnouin
TBF Génie Tissulaire
6 rue d'Italie
69780 Mions France
SME