GUIDELINE FOR THE NOMENCLATURE OF CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS' ACTIVE SUBSTANCES

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The identification of an investigational medicinal product requires at least a name for the medicinal product and at least a name for the active substance. The use of these names should be consistent in all clinical trial's documents, as well as in the documents related with compassionate use. Therefore, the names for the medicinal product and active substance should also be clearly identified in any adverse reaction notification and in the requests for inspections of the manufacturing facilities. In addition, the use of these names should be consistent in all clinical trials referring to the same medicinal product.

The supervision of both, safety and efficacy of cell therapy medicinal products in clinical trials is of paramount importance. To evaluate the available experience with this kind of medicinal products, a standardisation of nomenclature for their active substances is necessary.

The aim of this proposal is to set a standard as user-friendly and flexible as possible for the naming of the active substances before an official name is available, in such a way that, when clinical trials are conducted with the same type of active substance, the same name would be used in order to avoid any confusion.

In this scheme, each generic identification would consist of seven attributes each one selected from closed lists of terms that could be updated in the future as needed. In addition, one more free text attribute is included allowing the sponsor to indicate cellular subtype or other peculiarities as appropriate. Another attribute is included for cell-based gene therapy products describing the way the cells are genetically modified. The proposed terms have been selected taking into account the information requested in section D of the current Clinical Trial Application form for authorisation of a clinical trial in the EU. Some examples of active substances according to this proposal are given.

This modular approach would allow transparent and meaningful identification of the active substance before an official term is available and it would simplify searches in clinical trials and marketed products databases.

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The name of the active substances for cell therapy medicines will be formed by the juxtaposition of terms corresponding to the following nine attributes, the last two of them to be used when applicable:

1. Relation to the patient: alogenic, autologous and xenogenic.
2. Anatomical origin: adipose tissue, amniotic fluid, amniotic membrane, bone marrow, cartilage, conjuctiva, cornea, dental pulp, mucose, muscle, pancreas, peripheral blood, periosteum, placenta, sclerocorneal limbus, sinovial fluid, skin, umbilical cord, umbilical cord blood.
3. Differentiation status: differentiated, stem[1].
4. Source: adult, embryonic, foetal, iPS[2].
5. Cellular type: B lymphocytes, cardioblasts, chondrocytes, dendritic, endothelial, epitelial, erythrocytes[3], fibroblasts, hematopoietic, hepatocytes, keratinocytes, keratocytes, limbal, macrophages, melanocytes, mesenchymal, myoblasts, myocytes, mononuclear, neural, NK, osteoblasts, pancreatic, placental, T lymphocytes.
6. Product class: cells, islets, cell-sheet.
7. Manipulation: expanded, not expanded.
8. Specific data: free text information considered of interest by the sponsor: cell sub-type (e.g. CD133, CD34+), derived from…., stimulated with…, incubated with…, selected with…, combined with (in the case of a medical device), etc.
9. Genetic modification: Infected with…, transfected with…

Group 6 of attributes will only be used if it is not already implicit in the term of group 5. However, groups 5 and 6 of attributes will be used together when needed, as “mesenchymal cell”.

Groups 8 and 9 will only be used if applicable.

Suggestions in relation with these lists of terms should be submitted by e-mail to aecaem@aemps.es and dbiologicos@aemps.es indicating in the subject “Cell therapy nomenclature”.

Examples of names formed with this scheme

Autologous cartilage differentiated adult chondrocytes expanded.

Autologous bone marrow stem adult mesenchymal cells non expanded.

Autologous fat stem adult mesenchymal cells expanded combined with matrix…

[1] This term will be considered equivalent to “progenitors”.
[2] This term will be considered equivalent to induced pluripotent stem cells.
[3] This term will be considered equivalent to “red cells”.

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Autologous peripheral blood differentiated adult dendritic cells expanded pulsed with…

Alogenic skin differentiated adult fibroblasts expanded in matrix…

Alogenic sclerocorneal limbus stem adult limbal cells expanded over amniotic membrane.

Autologous bone marrow stem adult mononuclear cells non expanded.

Autologous peripheral blood differentiated adult NK cells expanded stimulated with…

Autologous skeletal muscle stem adult myoblasts expanded.

Alogenic umbilical cord blood stem foetal hematopoietic cells expanded CD34+.

Annex

During the consultation period two topics of special interest came out:

1. The cellular type in some products is not well defined and it can be considered that these products contain a mixed cell population what could render category 5 meaningless. Our position is that for every product, it should be defined the cellular type responsible for the mechanism of action (no matter how hypothetical it could be); the rest of the cellular components should be considered as impurities. However, a product could contain more than one cellular type, in which case each one should be defined following this proposed approach.

2. In some cases, certain attributes could seem redundant. However, it would be preferable to keep them in order to facilitate searches. i.e., although in some cases the anatomic origin is obvious, it should be maintained: in “liver hepatocytes” the liver origin is implicit in the term hepatocyte. However, maintaining liver will allow retrieving clinical trials with cell therapy products based on any type of liver cells.

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