INN Working Doc. 20.478
May 2020
Distr.: GENERAL
ENGLISH ONLY

Cell-based therapies:
Mandatory information for INN selection and publication

ANNEX TO INN APPLICATION FORM

Geneva, May 2020

Programme on International Nonproprietary Names (INN)

INN Programme and Classification of Medical Products Unit
Health Products Policy and Standards Department (HPS)
Access to Medicines and Health Products Division (MHP)
World Health Organization, Geneva

INN Working Doc. 20.478
May 2020
Distr.: GENERAL
ENGLISH ONLY

Mandatory information for INN selection and publication for cell-based therapies including cell-based gene therapy substances

Annex to INN application form

(Please note that incomplete requests will not be considered)

1. Laboratory code name(s) and/or other code name used in publications and clinical trials

2. **Cell source or tissue of origin**

    a. Where a cell therapy product or substance is prepared from a cellular source, a description of the starting cell material should be provided, for example, isolation from peripheral blood or apheresis material, with some characterisation of the cellular subpopulations within the starting material.

    b. Where a starting cell material is derived from a Cell Bank, information on its derivation and characterization should be provided.

    c. Where a substance is initially extracted from tissue, a description of the starting tissue material should be provided, as well as the process for extraction of the cells.

    d. Where there is no further processing or manipulation of the cells, section 3 must still be completed.

3. Outline the **key steps of the manufacturing process,** including any manipulations.

    a. Describe any cell enrichment or purification/selection of the starting material or performed on the cells at any step at in the preparation of the drug product or substance.

    b. Provide a list and details of any *in vitro* culture conditions, including those used during genetic modification of the cells, cell activation and differentiation, number of passages and/or population doublings.

    c. Describe any in-process holding steps and the finished product storage conditions, if applicable.

4. **Characterization/description of the substance**

    a. A detailed description of the substance should be provided. This includes, but is not limited to the cell identity, purity (identifying all major cell populations), activation state of the critical cell type(s), if they have been antigen loaded, and potency (if appropriate). The identity of the main cell populations should be described at both the phenotypic level (cell surface expression profile, using a minimum of 2 cell surface markers) and functional level, where available.

b. Where the substance is claiming to be a **stem cell** to act therapeutically, additional in vitro and/or in vivo information must be provided to demonstrate that the cells are capable self-renewal, are unspecialized, and the population can give rise to a number of specialized cell types.

c. Where the substance is claiming to be composed of **stem or progenitor cells** to act therapeutically, additional in vitro and/or in vivo data must be provided to demonstrate the claimed cell functionality/ies.

d. Where the substance is claiming to be composed of **stromal cells** to act therapeutically, additional in vitro and/or in vivo data must be provided to demonstrate the claimed cell functionality/ies.

It is up to the applicant to decide the best analytical methods and markers used to characterize the substance. Justification of the phenotype should be carefully considered.

5. If **genetic manipulation**: the detailed description of the vector and insert should be provided.

   a. The **full nucleotide sequence** of the substance in the following format: 50 nucleotides per line, in blocks of 10, with numbering at the end of each line in a format that can be copied (Word or in the text of an e-mail).
   The nucleotide sequence should be annotated to delineate relevant parts of the sequence (e.g. coding regions, control regions).

   b. A **table of features** providing an overview of the relevant parts of the sequence. The table should contain the annotation, a description of the annotation, the position and the colour code used in the sequence. Where a new vector is derived from an existing one, a sequence alignment and table of comparison should be provided.

   c. A **schematic map** of the entire nucleic acid showing inserted/deleted gene(s) and relevant functional parts.

   d. If the manipulation has an impact on the characteristics of the cell population (e.g. modification of a known gene function or cell de-differentiation), this