Common Application form for clinical research with human cells genetically modified by means of retro/lentiviral vectors[1]

NOTE 1: This application form can only be used for human cells genetically modified by means of retro/lentiviral vectors in cases where the applicant demonstrates that:
(1) there is no risk of formation of replication competent virus, and
(2) the finished product is free of infectious viral vector particles that are capable of being released in the environment.

NOTE 2: This application form can be used for submissions in the following jurisdictions: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Luxembourg, Malta, the Netherlands, Portugal, Romania, Spain, Sweden, and Norway.

NOTE 3: The application form must be accompanied by the SNIF (summary notification information format for notifications concerning the deliberate release into the environment of genetically modified organisms for purposes other than for placing on the market)[2] in the case of submissions that are made under Directive 2001/18/EC.

Document history	Publication Date	Description of main changes
Version 1	July 2018	
Version 2	December 2018	Endorsement by additional Member States (EE, FI, IE, SE)
Version 3	October 2019	Endorsement by additional Member States (CZ, LV, NL). Presentation of confidential information (to be submitted in an Annex.)

[1] This document has not been adopted by the European Commission and, therefore, it does not contain the official position of the European Commission.
[2] Council Decision 2002/813/EC establishing, pursuant to Directive 2001/18/EC of the European Parliament and of the Council, the summary notification information format for notifications concerning the deliberate release into the environment of genetically modified organisms for purposes other than for placing on the market (OJ L 280,18.10.2002, p.62)

COMMON APPLICATION FORM FOR CLINICAL RESEARCH WITH HUMAN CELLS GENETICALLY MODIFIED BY MEANS OF RETRO/LENTIVIRAL VECTORS

SECTION 1 – ADMINISTRATIVE INFORMATION

1.1. Identification of the applicant:

Organisation Name:	
Address Details:	
Contact person:	
Telephone No:	
Email Address:	

1.2. Identification of the sponsor (to the extent that is different from the applicant):

Organisation Name:	
Address Details:	
Contact person:	
Telephone No:	
Email Address:	

1.3. Information about the clinical trial[3]:

a) General information about the clinical trial:

EudraCT-number (where available):	
Objective of the study:	
Intended start and end date:	

[3] For applications submitted in Sweden -where a single submission procedure has been put in place- only the Eudra CT-number is mandatory.

Number of trial subjects that will take part in the study:	
Indicate if an application related to the same investigational medicinal product has been submitted -or is planned to be submitted- to other EEA Member States. In the affirmative, please identify the countries concerned:	

b) Intended location(s) of the study:

The applicant should provide information about the sites located in the country of submission of the application. In addition to the location of the clinical activities,[4] the location(s) of laboratories[5] in which activities with the GMO are carried out under the terms of this application should be stated (e.g. location of storage of the investigational medicinal product, location of storage of samples from clinical trial subjects that contain GMOs).

Organisation Name:	
Address Details:	
Contact person:	
Telephone No:	
Email Address:	
Planned activities:	
Containment level:	
Name and contact details of the responsible person[6]:	

Organisation Name:	

[4] The location of the site(s) where donation, procurement and testing of the donor cells take place need not be listed.

[5] Laboratories that perform routine laboratory diagnostics analysis need not be listed.

[6] The responsible person is either the person responsible for supervision and safety as provided for under Annex V of Directive 2009/41/EC, or the responsible scientist as provided for under Annex IIIA of Directive 2001/18/EC.

Address Details:	
Contact person:	
Telephone No:	
Email Address:	
Planned activities:	
Containment level:	
Name and contact details of the responsible person:	

(Applicant should complete as many tables as necessary)

c) Logistics for transportation:

The applicant should provide information about the logistics for in-house transportation.

SECTION 2 –INFORMATION ABOUT THE INVESTIGATIONAL MEDICINAL PRODUCT

2.1 Characterisation of the finished investigational medicinal product.

a) General information:

Description of the finished medicinal product	Autologous ☐ Allogeneic ☐
	Specify type of cells (*e.g*. hematopoietic stem cells…): ……
	Viral vector used: Retrovirus ☐ Lentivirus ☐
Pharmaceutical form:	
Mode of administration:	

b) Absence of replication competent virus particles in the finished product:

The applicant should demonstrate absence of formation of replication competent virus at the level of the viral production system or, alternatively, demonstration of absence of replication

competent virus in the transduced cells in accordance with the Good Practice on the assessment of GMO-related aspects in the context of clinical trials with human cells genetically modified by means of retro/lentiviral vectors.

Confidential information should be provided in an annex, together with the reasons why it is considered confidential. The Section of the application form to which the information refers should be clearly identified. When confidentially is claimed, a summary that can be made public should be provided in this section.

c) Absence of residual infectious viral vector particles in the transduced cells:

The applicant should demonstrate that residual infectious retro/lentiviral particles have been reduced to negligible concentrations in accordance with the Good Practice on the assessment of GMO-related aspects in the context of clinical trials with human cells genetically modified by means of retro/lentiviral vectors.

Confidential information should be provided in an annex, together with the reasons why it is considered confidential. The Section of the application form to which the information refers should be clearly identified. When confidentially is claimed, a summary that can be made public should be provided in this section.

2.2. Molecular characterisation of the applied vectors.

a) Map of the construct:

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b) Description of each of the components of the vector:

The applicant should provide a detailed description of each of the components of the vector used.

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should be clearly identified. When confidentially is claimed, a summary that can be made public should be provided in this section.

SECTION 3- CONTROL MEASURES

3.1. Measures to prevent risks of accidental transfer during administration to health care professionals and other staff involved in the transport/handling/administration of the product:

The applicant should provide an overview of relevant (hospital hygiene) measures that will be taken, including personal protective equipment and a description of measures to take in case of accidental self-administration of the investigational medicinal product (e.g. needle stick).

3.2. Risk minimisation strategies regarding patients:

The applicant should explain if it is considered that patients should be prevented from donating blood/cells/tissues/organs after being administered the genetically modified human cells.

3.3. Measures to prevent dissemination into the environment:

Decontamination/cleaning measures after administration:	
Elimination or inactivation of left-overs of the finished product at the end of the clinical trial:	
Waste treatment:	

3.4. Other risk minimisation measures:

This section should only be completed if the applicant considers that there are additional risk minimisation measures that should be implemented.

Identified risk(s)	Risk minimisation measure(s)

SECTION 4- ENVIRONMENTAL RISK ASSESSMENT

Specific environmental risk assessment:

Considering the specific characteristics of the investigational medicinal product (as described in Section 2), the applicant considers that the specific environmental risk assessment provided for in the *Good Practice on the assessment of GMO-related aspects in the context of clinical trials with human cells genetically modified by means of retro/lentiviral vectors* is applicable:

Yes ☐

No ☐

If the answer to the above is "No", the following information should be provided:

- *For submissions made under Directive 2001/18/EC*: an environmental risk assessment is required in accordance with Annex II thereof.

- *For submissions made under Directive 2009/41/EC*: an assessment of the risks to human health and the environment in accordance with Article 4 thereof.

SECTION 5 - MANUFACTURE OF THE INVESTIGATIONAL MEDICINAL PRODUCT

5.1. Manufacturing site:

Organisation Name:	
Address Details:	
Contact person:	
Telephone No:	
Email Address:	
License number: (if the site is not in the country of application, please indicate the country where the manufacturing takes	

place)	
Containment level:	

5.2. Application for manufacturing license:

This Section should only be completed if the applicant is also responsible for the manufacturing of the investigational medicinal product and seeks authorisation of the manufacturing site responsible for the transduction of the cells or other downstream manufacturing activities.

Please note that the possibility to request for (simultaneous) authorisation for manufacturing activities and for the conduct of the clinical trial by means of this application form is only available in Cyprus, Czech Republic, Greece, Hungary, Italy, Malta and Romania. For submissions outside these jurisdictions Section 5.2 should not be filled in.

a) Administrative information about the site:

Organisation Name:	
Address Details:	
Contact person:	
Telephone No:	
Email Address:	

b) Description of manufacturing operations and risk minimisation measures:

Information about the vector production system
b.1. The production cell line contains HIV 1 or 2, HTLV 1 or 2, SIV or other relevant retro-lentivirus that could lead to complementation/recombination of the retro/lentiviral vector: Yes ☐ No ☐ b.2. Cells from HIV/HTLV positive donors are excluded: Yes ☐ No ☐ b.3. Please provide a detailed description of the each of the components of the vector and characterisation of the critical elements of the helper/packaging vectors. *Confidential information should be provided in an annex, together with the reasons why it is considered confidential. The Section of the application form to which the information refers should be clearly identified. When confidentially is claimed, a summary that can be made public should be provided in this section.*

b.4. Deviations from the predicted sequences have been identified at the level of molecular characterisation of the applied vectors. In the affirmative, please provide details.

Yes ☐

No ☐

Description of manufacturing operations
Confidential information should be provided in an annex, together with the reasons why it is considered confidential. The Section of the application form to which the information refers should be clearly identified. When confidentially is claimed, a summary that can be made public should be provided in this section.

Risk minimisation measures

c) Level of containment:

SECTION 6- OTHER DATA REQUIREMENTS

6.1. Plan of the site(s) concerned:

Applicant should provide a copy of the plan of the site where the clinical trial takes place if the application is submitted to the following jurisdictions: Austria, Czech Republic, Finland, France, Hungary, Italy, Portugal or Norway.

Applicant should provide a copy of the plan of site where manufacturing activities take place (if the application covers manufacturing activities, i.e. Section 5.2) in case the application is intended for Czech Republic, Italy or Hungary.

6.2 Other information:

***For submissions to Italy**:*

The applicant should, in addition to the plan of the site, provide information on the location of the autoclave used for the purposes of waste treatment and inactivation (applications that cover manufacturing activities). If the application only covers the conduct of the trial but not manufacturing, a description of the location of the autoclave should be provided –as appropriate- as part of the description of the measures to prevent dissemination into the environment (section 3.3).

For submissions to the Netherlands:

More information on national procedural requirements and forms is available at: https://www.loketgentherapie.nl/en/gm-cells

***For submissions to Romania that cover manufacturing activities**:*

The applicant should provide the GNSS (global navigation satellite system) coordinates of the site(s) where the concerned manufacturing activities take place.