EU Official Control Authority Batch Release

Human Vaccines

Guideline for Pandemic COVID-19 Vaccine (Non-replicating Adenovirus-vectored vaccine)

New Guideline
In force from 01/05/2021

European Commission
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé
COUNCIL OF EUROPE
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Document title	Official Control Authority Batch Release Of Pandemic COVID-19 Vaccine (Non-replicating adenovirus-vectored vaccine)
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Custodian organisation	The present document was elaborated by the EDQM in the OMCL network and finalised under PA/PH/OMCL (21) 29 DEF

OFFICIAL CONTROL AUTHORITY BATCH RELEASE OF PANDEMIC COVID-19 VACCINE (NON-REPLICATING ADENOVIRUS-VECTORED VACCINE)

1. Introduction

Control Authority Batch Release of immunological medicinal products is performed within the framework of Article 114 paragraph 1 of Directive 2001/83/EC and Article 1 paragraph 78 of the amending Directive 2004/27/EC and following the current guideline on EC administrative procedure for Official Control Authority Batch Release.

All general and specific Ph Eur monographs pertaining to this product apply.

2. Sampling and tests to be performed by the Control Laboratory

The following samples should be supplied to the Official Medicines Control Laboratory performing batch release:

At least 20 single/multi dose containers of each final lot

The Control Laboratory should perform the following tests:

On the final lot:

- Appearance
- Potency
- Identity (potency may serve as an identity test)

3. Protocol submission

The protocol submitted by the manufacturer should reflect all appropriate production steps and controls for a particular product as outlined in the Marketing Authorisation for that specific product. A **MODEL** protocol is given below to help ensure complete and harmonised protocol submission. An attempt has been made to list all appropriate production steps and controls as required by the various Marketing Authorisations and the relevant monograph(s) of the Ph Eur for products of this type. The manufacturer should omit listed items that are not required by his Marketing Authorisation and include any relevant additional items. It is thus possible that **a protocol for a specific product may differ in detail from the model provided**. The essential point is that **all relevant details demonstrating compliance with the Marketing Authorisation and the Ph Eur monograph(s) (if available) for a particular product should be given in the protocol submitted**.
Results of the tests are required (passed or failed is not sufficient, initial results and, where applicable, results of retests should be given). Sufficient detail should be supplied to allow recalculation of test values. Specifications for each test and dates when the tests were performed should also be included. Results of qualification tests on reference materials should be given for each new in-house reference material.

3.1 Summary information on the finished product (final lot)

Trade name: ……

International non proprietary name (INN) / Ph Eur name /Common name of product (whichever is appropriate): ……

Batch number(s):

Finished product (final lot): ……

Final bulk: ……

Type of container: ……

Total number of containers in this batch: ……

Number of doses per container: ……

Composition/volume of single human dose: ……

Date of expiry: ……

Date of start of period of validity: ……

Storage temperature: ……

Marketing authorisation number: ……

Marketing authorisation number issued by: (Member state/EU): ……

Name and address of manufacturer: ……

Name and address of Marketing Authorisation Holder if different: ……

3.2 Production information

Site of manufacture: ……

Date of manufacture: ……

Summary information scheme on batch specific production data including dates of different production stages, different production site(s) where relevant, identification numbers and blending scheme.

3.2.1 Starting materials

The information requested below is to be presented on each submission. Full details on Master and working seed-lots and cell banks upon first submission only.

3.2.1.1 Virus seed lots

Reference number and strain origin of the adenoviral vector used to prepare the licensed COVID-19 vaccine ……

Master seed lot N° & preparation date: ……

N° of passages between two seeds mentioned above: ……

Date of approval of protocols indicating compliance with the requirements of the relevant Ph. Eur. monographs and with the Marketing Authorisation: ……

Working seed lot N° & preparation date: ……

Passage level from Master seed lot: ……

Date of approval of protocols indicating compliance with the requirements of the relevant Ph. Eur. monographs and with the Marketing Authorisation: ……

Sufficient detail as defined in the MA should be provided for any additional 'sub' working seed lots including the passage level from the master seed and the length and conditions of storage if any.

3.2.1.2 Cell substrate for virus propagation

Master cell bank (MCB) N° & preparation date: ……

Population doubling level (PDL) or passage of MCB: ……

Date of approval of protocols indicating compliance with the requirements of the relevant Ph. Eur. monographs and with the Marketing Authorisation: ……

Manufacturer's working cell bank (MWCB) N° & preparation date: ……

Population doubling level (PDL) or passage of MWCB: ……

Date of approval of protocols indicating compliance with the requirements of the relevant Ph. Eur. monographs and with the Marketing Authorisation: ……

Production cell lot N°: ……

Date of thawing ampoule of MWCB: ……

PDL or passage of production cells when inoculated with virus seed: ……

Identification of cell substrate: ……

Methods used: ……

Subculture of MWCB (if applicable)

N° & preparation date:

Population doubling level (PDL) or passage of MWCB: ……

Date of approval of protocols indicating compliance with the requirements of the relevant Ph. Eur. monographs and with the Marketing Authorisation: ……

Production cell lot N° ……

Date of thawing ampoule of MWCB: ……

PDL or passage of production cells when inoculated with virus seed: ……

Identification of cell substrate: ……

Methods used: ……

Identification and source of starting materials used in preparing production cells including excipients and preservatives (particularly any materials of human or animal origin e.g. albumin; serum, trypsin etc.): ……

3.2.1.3 Control cell cultures

Provide information on control cells corresponding to each single harvest.

Ratio or proportion of control to production cell cultures: ……

Period of observation of cultures: ……

Percentage rejected for non-specific reasons: ……

Result: ……

Identity (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Viability (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Bioburden (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Extraneous viral agents

Information on extraneous viral agents testing as approved in Marketing Authorisation and in line with Ph. Eur chapter 2.6.16 should be reported below including details on test system (method, volume tested, incubation time and temperature, dates, results and as appropriate cell line/animal, anti-sera, media used, etc)

3.2.2 Intermediate stages

3.2.2.1 Purified bulk

Information on each stage of the drug substance manufacturing process (including where applicable cell expansion with control cells, virus harvest, clarification, chromatography…): date of production, batch number, volume, storage temperature, storage time and approved storage period, methods and results of the in-process controls

Batch N°(s): ……

Date(s) of manufacture: ……

Volume(s), storage temperature, storage time and approved storage period: ……

Identity
Method: ……
Specification: ……
Date: ……
Result: ……

Virus protein Fingerprinting (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Host cell Protein
Method: ……
Specification: ……
Date: ……
Result: ……

Host cell DNA
Method: ……
Specification: ……
Date: ……
Result: ……

DNA/protein ratio (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Residual benzonase (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Infectious units
Method: ……
Specification: ……
Date: ……
Result: ……

Transgene Expression
Method: ……
Specification: ……
Date: ……
Result: ……

Ratio Virus Particles / Infectious units
Method: ……
Specification: ……
Date: ……
Result: ……

Virus particles
Method: ……
Specification: ……
Date: ……
Result: ……

Bacterial endotoxin
Method: ……
Specification: ……
Date: ……
Result: ……

Bioburden
Method: ……
Specification: ……
Date: ……
Result: ……

Replication Competent Adenovirus
Method: ……
Specification: ……
Date: ……
Result: ……

pH
Method: ……
Specification: ……
Date: ……
Result: ……

Osmolality (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Appearance
Method: ……
Specification: ……
Date: ……
Result: ……

Polysorbate 80 Concentration (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

3.2.2.2 Final bulk

Batch N°: ……

Batch number and volume of purified bulk(s) used: ……

Other substances added and volumes: ……

Date of blending: ……

Bioburden (if applicable)

Method: ……

Specification: ……

Date: ……

Result: ……

3.3 Batch of finished product (final lot)

Batch N°: ……

Date of filling: ……

Date of freezing: (if applicable) ……

Freezing t°(if applicable) ……

Type of container: ……

Filling volume: ……

Number of containers after inspection: ……

Appearance

Method: ……

Specification: ……

Date: ……

Result: ……

Identity

Method: ……

Specification: ……

Date: ……

Result: ……

Virus protein fingerprinting (if applicable)

Method: ……

Specification: ……

Date: ……

Result: ……

pH
Method: ……
Specification: ……
Date: ……
Result: ……

Sterility
Method: ……
Media: ……
Volume inoculated: ……
Date test on: ……
Date test off: ……
Result: ……

Infectious units
Method: ……
Specification: ……
Date: ……
Result: ……

Transgene expression
Method: ……
Specification: ……
Date: ……
Result: ……

Ratio virus particles/ Infectious units
Method: ……
Specification: ……
Date: ……
Result: ……

Virus particles
Method: ……
Specification: ……
Date: ……
Result: ……

Bacterial endotoxins
Method: ……
Specification: ……
Date: ……
Result: ……

Aggregates (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

DNA/Protein ratio (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Extractable volume
Method: ……
Specification: ……
Date: ……
Result: ……

Osmolality
Method: ……
Specification: ……
Date: ……
Result: ……

Polysorbate 80 concentration
Method: ……
Specification: ……
Date: ……
Result: ……

Container closure integrity (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Sub visible particles (if applicable)
Method: ……
Specification: ……
Date: ……
Result: ……

Date of start of period of validity ……

4 Certification

Certification by qualified person taking the overall responsibility for production and control of the product:

I herewith certify that _____(name of the product) batch N°_____ was manufactured and tested according to the procedures approved by the competent authorities and complies with the quality requirements. This includes that, for any materials derived from ruminants (bovine, ovine, caprine) used in the manufacture and/or formulation of the batch of product specified above, all measures have been taken to demonstrate compliance with Directive 2001/83/EC and amending Directives 2003/63/EC and 2004/27/EC.

In addition the OMCL performing OCABR has been notified of all relevant approved variations that have an impact on product specifications or on data supplied in section 3 of this protocol as described in the EU administrative procedure for OCABR.

Name: _____

Function: _____

Date: _____

Signature:_____