EU Official Control Authority Batch Release,

Official Batch Protocol Review

Immunological Veterinary Medicinal Products

**Manufacturer’s Protocol Model Template for Live Bacterial Vaccines**

**This version in force from 28 January 2022**

**Replacing version in force from 1 April 2007**

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| **Document title** | Manufacturer’s protocol for submission of an IVMP to a Competent Authority for OBPR/OCABR: Model format for live bacterial vaccines |
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| **Custodian organisation** | The present document was elaborated by the EDQM through the OMCL network and is presented as adopted under PA/PH/OMCL (21) 127 DEF |

**MANUFACTURER’S PROTOCOL FOR SUBMISSION OF AN IVMP TO A COMPETENT AUTHORITY FOR OBPR/OCABR**

**MODEL FORMAT FOR LIVE BACTERIAL VACCINES**

To ensure a harmonised presentation the following template should be used when submitting protocols to a Competent Authority (CA)/Official Medicines Control Laboratory (OMCL) for Official Batch Protocol Review (OBPR) or Official Control Authority Batch Release (OCABR).

A completed and signed protocol should be provided by the Marketing Authorisation Holder (MAH), to the CA or designated OMCL performing OBPR or OCABR for any given batch.

For OCABR the samples of each batch to be controlled should also be provided to the OMCL performing OCABR.

***The* *information required for each type of product will vary and the following template is intended as a guide****.*

Section 1 ‘Member State specific information’ and 2, the ‘summary information on the final batch’ should be presented in the format shown so as to facilitate the preparation of an Official Control Authority Batch Release certificate, or Official Batch Protocol Review certificate of approval.

The protocol submitted by the MAH 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 appropriate production steps and controls as required by the various Marketing Authorisations and the relevant monograph(s) of the European Pharmacopoeia (Ph Eur) for products of this type.

Items listed in the model that are not required by the relevant Marketing Authorisation should be omitted, equally, items not listed that are required by the Marketing Authorisation should be included.

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 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 the results in the determination of the potency or quantity of the active ingredient. Specifications for each test and dates when the tests were performed should also be included. Results of qualification tests on reference materials that are used for the calculation of test results in the determination of the potency or quantity of the active ingredient should be given for each new in-house reference material of this type.

**1 MEMBER STATE SPECIFIC INFORMATION**

**Antigen-containing component(s):**

Identification number for batch to be placed on the market

in the Member State (if packaging number

different from final batch number in section 2): ........................................

Marketing authorisation number issued

by (Member State/EU): ........................................

Target species: ........................................

Total number of containers in this batch: ........................................

Number of containers the release is applied for: ........................................

Number of doses per container: ........................................

Number of samples for the competent authority: ........................................

Date of expiry: ........................................

Name and address of Marketing Authorisation

Holder (if different from manufacturer in section 2): ........................................

**Diluent (if applicable):**

Trade name (if applicable): ........................................

Batch number of diluent

to be used in the Member State

(if different from that in section 2): ........................................

Type of final container: ........................................

Total number of containers in this batch: ........................................

Number of containers the release is applied for: ........................................

Number of doses/volume per container: ........................................

Number of samples for the competent authority: ........................................

Date of expiry: ........................................

**2 SUMMARY INFORMATION ON THE FINAL BATCH OF FINISHED PRODUCT**

Trade name: ........................................

International non-proprietary name (INN)/Ph Eur name/ common name

of product (whichever is appropriate): ........................................

Batch number(s) of: Finished product (final batch): ........................................

Final bulk: ........................................

Pharmaceutical form of finished product: ........................................

Type of final container: ........................................

Date of start of period of validity

(start of titration/potency test): ........................................

Storage temperature: ........................................

Name and address of manufacturer: ........................................

Name and address of the batch release site

(if different from that of manufacturer): ........................................

Diluent (if applicable):

Nature of diluent: ........................................

Batch number: ........................................

Name and address of batch release site: ........................................

Storage temperature: ........................................

**3 PRODUCTION INFORMATION**

Site of manufacture for each antigen (whenever

more than one production site exists): ........................................

The production protocol should follow the flow sheet and the outline of production given in the MA dossier. Provide here a summary information scheme on batch specific production data including dates of different production stages and identification numbers of components.

The overview of each step of production must be given for each component separately in section 3.2

**3.1 Starting materials**

3.1.1. Bacteria seed lots

master seed material: MS-batch number:

date of last testing:

working seed materials: WS-batch number:

date of last testing:

3.1.2. Substrates (if applicable)

3.1.2.1 Permanent cell line

master cell seed: ………………………………………….

MCS-batch number: ………………………………………….

date oflast testing: ………………………………………….

working cell seed ………………………………………….

WCS-batch number: ………………………………………….

date oflast testing: ………………………………………….

* 1. **Intermediate stages of production**

All production steps should be listed separately for each antigen-containing component outlined in section 3. The time frames as well as the clear identification of material involved in each step must be mentioned. Start and end dates of cell passaging should be included where appropriate.

Antigen-containing component:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Production step  (as required) | Start | End | Material | Volume | Other relevant  data as required |
| Such as…. |  |  |  |  |  |
| Seed |  |  |  |  |  |
| Harvest/ Clarification |  |  |  |  |  |
| Concentration |  |  |  |  |  |

#### If separate batches of harvest are combined before blending of the final bulk include details here:

Components (Harvest batch No): Volume:

Total volume of combined pool:

Start date and end date of pooling:

Batch number of the combined pool:

**3.3 CREATION OF THE FINISHED PRODUCT**

**3.3.1 BLENDING AND VACCINE COMPOSITION (Antigen-containing component)**

3.3.1.1.Blending of the final bulk:

Start and end date of blending:

3.3.1.2. Composition of the final bulk

Batch number of the final bulk:

Harvests/bulks of active components and excipients used to create the final bulk as appropriate:

Component Batch no. Final Volume Target Ratio.

Strain

Excipient

**3.3.2 FILLING**

Batch number of final bulk used for fill:

Final Batch number: Filling date: Number of filled container Vol.filled:

**3.3.3 LYOPHILISATION**

Final Batch number:

start: end:

Final Batch (or sub-batch) number: Number of containers

* 1. **IN PROCESS CONTROLS** (for antigen containing components)

(As indicated in the flow sheet of the Marketing Authorisation)

Relevant Ph Eur monograph(s) should be listed where appropriate. For each test indicate clearly which method was used and clearly identify the authorised test (refer to method identification number eg. SOP and version number or provide a clear, brief description). Provide identification number of the material tested.

Test: Start: End: Result: Thresholds: Conclusion

Such as…..

- assay for bacterial

growth of the excipients

- test for sterility of the excipients

- purity

- identity

- bacteria count

**3.5 Diluent (if applicable)**

3.5.1 Composition

Batch number:

Component Batch no. Total volume Final conc.

3.5.2 Filling

Batch number of material used for fill:

Final Product (batch) number: Filling date: Number of filled container Vol.filled:

3.5.3 Control Tests On The Diluent

Identification number of material tested:

Test: Start: End: Result: Thresholds: Conclusion

Such as….

-appearance

-sterility

-filling volume

-chemical tests

-pH

-bacteriocidal effect

-viscosity

-density

1. **FINAL BATCH TESTING (finished product) (**Antigen-containing component)

Relevant Ph Eur monograph(s) should be listed where appropriate, the results of the relevant reference-preparations used for the calculation of test results for each test should be included. For each test indicate clearly which method was used and clearly identify the authorised test (refer to method identification number eg. SOP and version number or provide a clear, brief description).

Identification number of material tested:

Test: Start: End: Result: Thresholds: Conclusion

Such as…..

-appearance

- solubility

- purity

- live bacteria count

- identity

-safety

- water (residual moisture)

- vacuum testing (if applicable)

1. **Certification BY THE MANUFACTURER**

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 requirement and that all measures have been taken to demonstrate compliance with Regulation (EU) 2019/6.

# Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

# Function: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

# Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

# Signature:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_