FOOD AND DRUGS AUTHORITY GHANA

GUIDELINES FOR BATCH RELEASE OF VACCINES

RABIES VACCINE

FDA/BPU/BR-V/2013/01

1. Introduction

These guidelines outline the minimum Ghana Food and Drugs Authority Batch Release requirements for the registration of immunological products.

All general and specific monographs relevant to the product apply (Refer to section 112 of the Ghana Public Health Act 851).

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

The number of samples (in final containers) used for batch release laboratory test should be statistically justified.

The Control Laboratory should perform the following tests:

- Appearance
- Antigen content by SRD test or ELISA test based on glycoprotein on every final lot
- NIH test for potency on final lot: a reduced testing of one final lot out of ten final lots derived from one final bulk is acceptable.
- Bacterial endotoxins on every final lot
- Pyrogens test : a reduced testing of one final lot out of ten final lots derived from one final bulk is acceptable.

3. Protocol submission

A model protocol is given below. The protocol for a specific product may differ in detail but it is essential that all relevant details demonstrating compliance with the registration requirements and the official monograph should be given. WHO requirements may also serve as the model for the content and the presentation of the protocol data. Results of tests are required (pass or fail is not sufficient, results of re-tests if applicable should be given).

Sufficient detail should be supplied to allow re-calculation of test values. Specifications for each test and dates when they 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)

Proprietary, Commercial or Trade name: ……

International Non- proprietary Name (INN): ……

Common name of product: ……..

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: ……

Storage temperature: ……

Name and address of manufacturer: ……

Name and address of registration holder if different: ……

Human Albumin used in the production (if applicable): .....

- Lot number: ……
- Manufacturer: ……

(if this batch has been tested and released by a contracted laboratory, the release certificate should be provided): ……

3.2. Production information

Site of manufacture: ……

Date of manufacture: ……

Summary information scheme on batch specific production data including dates of different production stages, 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

Virus strain and reference number used to prepare your licensed rabies vaccine: ……

Master seed lot number & preparation date: ……..

Number of passages between two seeds mentioned above: ……

Date of approval of protocols indicating

compliance with the requirements of the relevant monographs and with the conditions of registration: …….

Working seed lot number & preparation date: …….

Passage level from Master seed lot: …….

Date of approval of protocols indicating compliance with the requirements of the relevant monographs and with the conditions of registration: …….

3.2.1.2 Cell substrate for virus propagation

Master cell bank (MCB) number & preparation date: ……

Population doubling level (PDL) of MCB: .....

Date of approval of protocols indicating compliance with the requirements of the relevant monographs and with the conditions of registration: ……

Manufacturer's working cell bank (MWCB) number & preparation date: …….

Population doubling level (PDL) of MWCB: …….....

Date of approval of protocols indicating compliance with the requirements of the relevant monographs and with the conditions of registration: ……...

Production cell lot number: ……...

Date of thawing ampoule of MWCB: ……...

PDL of production cells when inoculated with virus seed: ……..

Identification of cell substrate
Methods used: ……...

Nature and concentration of antibiotics used in production of cell culture maintenance medium: ……...

Identification and source of starting materials used in preparing production cells including excipients and preservatives (particularly any

materials of human or animalorigin e.g. albumin; serum): ……..

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: ……

Extraneous haemadsorbing viruses
Type(s) of red blood cell (rbc): ……
Storage time and temperature of rbc: ……..
Incubation time and temperature of rbc: ……
Percentage (%) culture tested: ……
Date test on: ……...
Date test off: ……...
Result: ……

Tests on supernatant fluids for other extraneous agents

Date of sampling from production cell cultures: ……..
Type of simian cells: ……..
Quantity of sample inoculated: ……..
Incubation temperature: ……..
Date test on: ……...
Date test off: ……...
Percentage (%) of viable culture at the end: ……
Result: ……

Type of human cells: ……...
Quantity of sample inoculated: ……...
Incubation temperature: ……...
Date test on: ……...
Date test off: ……...
Percentage (%) of viable culture at the end: ……
Result: ……

Type of human diploid cells: ……...
Quantity of sample inoculated: ……...

Incubation temperature: ……...
Date test on: ……...
Date test off: ..…….
Percentage (%) of viable culture at the end: ……
Result: ……

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

Test for sterility
Method: ……
Media: ……
Volume inoculated: ……
Date test on: ……
Date test off: ……
Result: ……

3.2.2. Intermediate stages

3.2.2.1 Single Harvests
Batch number (s): …….
Date of inoculation: …….
Date(s) of harvest: .....

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

Tests on viral suspension (before concentration, purification, inactivation)

Date of pooling: …….

Test for sterility
Method: …….
Media: …….
Volume inoculated: …….
Date test on: …….
Date test off: …….
Result: …….

Mycoplasma
Method: …….

Media: …….
Volume inoculated: …….
Date test on: …….
Date test off: …….
Result: …….

Test for virus concentration (infectious titre on cell cultures or on animals)

Method: ……
Specification: ……...
Date: ……
Result: ……

3.2.2.2 Concentrated purified inactivated harvest

Date of concentration: ……
Date and method of purification: ……...
Date and method of inactivation: ……...

Tests on viral suspension (after concentration, purification, inactivation)

Test for effective inactivation
Amplification test: ……
Specification: ……...
Date: ……
Result: ……
Direct inoculation: ……...
Specification: ……...
Date: ……
Result: ……

Residual DNA
Method: ……
Specification: ……...
Date: ……
Result: ……

Residual bovine albumin content
Method: ……
Specification: ……...
Date: ……
Result: ……

Test for sterility

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

Mycoplasma
Method: …….
Media: …….
Volume inoculated: …….
Date test on: …….
Date test off: …….
Result: …….

3.2.2.3 Final bulk

Batch number(s): …….

Date of manufacture: ……

Volume, storage temperature, storage time and approved storage period: ……

Human albumin used in the manufacturing process: ……

-Lot number(s): ……
-Manufacturer: ……
Date of release by manufacturer: ……
Stage in the manufacturing process in which this lot (s) is used: ……

The information on excipients derived from human blood (e.g. albumin) should not be less detailed than the information requested for an active ingredient regarding documentation of starting materials as well as specifications and tests on the final product.

Glycoprotein content
Method: ……...
Specification: ……...
Date: ……...
Result: ……...

Test for sterility
Method: ……...

Media: ……...
Volume inoculated: ……...
Date test on: ……...
Date test off: ……...
Result: ……...

3.3. Batch of finished product (final lot)

Batch number: ……...

Date of filling: ……...

Type of container: ……...

Number of containers after inspection: ……...

Filling Volume: ……...

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

Residual moisture
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

Residual bovine albumin content
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

Protein content
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

Test for sterility
Method: ……...

Media: ……...
Volume inoculated: ……...
Date test on: ……...
Date test off: ……...
Result: ……...

Pyrogen assay
Method: ……...
Specification: ……...
Date: ……...
Result: ……...

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

Potency test
Species, strain, sex and weight specifications: …….
Challenge Dose (dilution): …….
Dates of vaccination: …….
Date of assay: …….
Batch number of reference vaccine + assigned potency: …….
ED_{50} of reference and test vaccine: …….
Potency of test vaccine (ED_{50} dilution): …….
Validity criteria: ……
Results: .....

Potency test *(in vitro)*
Date of assay: …….
Batch number of reference: …….
Assigned potency of reference: ……
Validity criteria: ……
Results: ……

Date of start of period of validity: …….

4.0. 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 number_____ 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 that the material is free from transmissible spongiform encephalopathy.

Name: _____

Designation: _____

Date: _____

Signature: _____