FOOD AND DRUGS AUTHORITY GHANA

GUIDELINES FOR BATCH RELEASE OF VACCINES

MEASLES 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 tests should be statistically justified.

The Control Laboratory should perform the

following tests:

- Assay (potency) and temperature stability
- Appearance
- Identity

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 requirement 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 seed 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 measles vaccine: ……..

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

Number of passages between two seed lots 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

3.2.1.2.1 If vaccine is produced on human diploid cells 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 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 animal origin e.g. albumin; serum): …….

3.2.1.2.2 If vaccine is produced on chicken embryos or chick embryo cells

Provide all information about the specific-pathogen-free healthy flock used as the source of the cells.

Tests for infections
Method: ……
Specification: ……
Date: ……
Result: ……
Date of certification: ……

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

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

Additional tests for avian viruses for production on chick embryo cells:

Test for Avian Leukosis Virus

Method: ……
Volume of sample inoculated: ……...
Date test on: ……...
Date test off: ……...
Result: ……...

Test for other avian viruses
Method: ……...
Type and batch number of avian cells: ……...
Volume of sample 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: ……...

Report results of tests for each single harvest.

Test for sterility

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

3.2.2.2 Pooled harvests before clarification

Batch number(s): ……....
Date(s) of pooling and clarification: ……....
Number, dilution medium, volume(s), storage temperature, storage time and approved storage period: ……...

Mycoplasma

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

Tests for mycobacterium spp.

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

Tests for extraneous agents

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 diploid cells (if vaccine produced on this cell type):

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

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

Virus concentration
Date of inoculation: ……..
Cells used for titration: .....
Reference preparation: ……..
Result: ……..

Additional tests for avian virus for production on chick embryo cells:

Test for Avian Leukosis Virus
Method: ……..
Volume of sample inoculated: ……..
Date test on: ……..
Date test off: ……..
Result: ……..

Test for other avian virus

Method: ……..
Type and batch number of avian cells: ……..
Volume of sample inoculated: ……..
Date test on: ……..
Date test off: ……..
Result: ……..

Embryonated chicken eggs
Allantoic route
Method: ……..
Volume of sample inoculated: ……..
Date test on: ……..
Date test off: ……..
Result: ……..

Yolk sack route
Method: ……..
Volume of sample inoculated: ……..
Date test on: ……..
Date test off: ……..
Result: ……..

3.2.2.3 Pooled harvests after concentration and clarification

Batch number(s): …….
Date(s) of concentration and clarification: …….
Volume(s), storage temperature, storage
time and approved storage period: ……

Test for Human Serum Albumin or Bovine Serum Albumin content
Method: ……..
Specification: ……...
Date: ……...
Result: ……...

Test for removal of intact cells

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

Residual antibiotic content
Calculation: ……..
Specification: ……..
Date: ……..
Result: ……..

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

Virus concentration
Date of inoculation: ……..
Cells used for titration: ……..
Reference preparation: ……..
Result: ……..

Additional test for production on chick embryo cellsOvalbumin
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

3.2.2.4 Final bulk
Batch number: …….
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.

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: ……
Date of freeze-drying: ……
Freezing temperature: ……
Drying period: ……
Type of container: ……
Filling volume: ……
Number of containers after inspection: ……

Appearance

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

Identity

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

pH

Method: ……
Specification: ……
Date: ……

Result: …….

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

Abnormal toxicity
Method: …….
Specification: ……
Date: ……
Result: ……

Bovine Serum Albumin
Method: ……
Specification: ……
Date: ……
Result: ……

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

Additional test for production on chick embryo cells Ovalbumin
Method: ……....
Specification: ...……...
Date: ...…….....
Result: …….....

Assay
-Date of inoculation: ……..…..
-Type of cell culture: ……
-Virus concentration

for each replicate vial
of vaccine under test
95% fiducial limits of
mean: ……

-Virus concentration
for each replicate vial after
storage for 7 days at 37°C
95% fiducial limits of mean: ……

-Virus concentration
for each replicate vial
of reference vaccine
95% fiducial limits of mean: ……

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 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: _____