FOOD AND DRUGS AUTHORITY GHANA

GUIDELINES FOR BATCH RELEASE OF VACCINES

POLIO 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:

- Identity and Assay (the assay serves as an identity test).

- *in vitro* assay used to determine the D Antigen content, must be done on the final lot.

- *in vivo* assay used to determine the ED_{50}, must be done on the final bulk or the first final lot filled from it.

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: ……...

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, virus type and reference number used to prepare your licensed inactivated poliomyelitis vaccine: …….

Master seed lot number & preparation date (one per package): …….

Number of passages between two seeds mentioned above: ……

Dates of approval of master virus seed lot protocols indicating compliance with the requirements of the relevant monographs and with the conditions of registration: ……

Working seed lot number & preparation
date (one per serotype):

Passage level from Master seed lot: ……

Dates of approval of working virus seed lot 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 continuous cells or 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 primary monkey kidney cells

Monkey species and origin: …….
For each monkey, Date of perfusion of kidneys: …….
For each monkey Test for Tuberculin sensitivity: …….
For each monkey Test for the absence of
antibodies (SV40, Herpes B, SIV and Foamy virus): .....

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: ……..
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: ……..

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: ……..

Additional tests on the neutralised supernatant fluid if monkey kidney cells are used.

In cercopithecus monkey kidney cell cultures sensitive for SV40

Quantity of sample inoculated: ……..
Incubation temperature: ……..
Date test on: ……..
Date test off: ……..
Percentage of viable culture at the end: ……..
Result: ……..

Test for Herpes B virus in rabbit kidney cell cultures
Quantity of sample inoculated: ……..
Incubation temperature: ……..
Date test on: ……..

Date test off: ……..
Percentage of viable culture at the end: ……...
Result: ……...

3.2.2 Intermediate stages

3.2.2.1 Single Harvests
Batch number(s) and virus type: ……...
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: ……

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

Test for Virus concentration (infectivity or D antigen determination)
Method: ……
Cells used (if applicable): ……
Specification: ……
Date: ……
Result: ……

Additional tests on the supernatant fluid if monkey kidney cells are used.

In cercopithecus monkey kidney cell cultures sensitive for SV40

Quantity of sample inoculated: ……....
Incubation temperature: ……....
Date test on: ……...
Date test off: ……..
Percentage of viable cells at the end: ……..
Result: ……....

Test for Herpes B virus in rabbit kidney cell cultures
Quantity of sample inoculated: …….
Incubation temperature: …….
Date test on: …….
Date test off: …….
Percentage of viable cells at the end: …….
Result: …….

3.2.2.2 Purified virus harvest
Batch number(s) and virus type: …….....
Date(s) of purification: …….
Volume(s), storage temperature, storage time
and approved storage period: …….

Report results of tests for each purified virus harvest, using extra pages if necessary.

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

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

D antigen content
Method: …….
Specification: …….
Date: …….
Result: …….

Protein content

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

Specific activity
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

Residual protein purification marker
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

Test for residual host-cell DNA (if continuous cells are used for production)

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

3.2.2.3 Inactivated monovalent bulk

Report results of tests for each inactivated monovalent bulk.

Batch number (s) and virus type: ……..
Date of manufacture: ……..
Volume, storage temperature, storage
time and approved storage period: ……..

Physico-chemical controls
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

D antigen content
Method: ……..
Specification: ……..

Date: ……..
Result: ……..

Purity: Ratio Protein/D antigen unit: ……..

Test for sterility

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

Details on inactivation process

Method: …….
Volumes of all preparatory and inactivation steps: …….
Inactivation curves of each harvest: …….
Specification: …….
Dates: …….
Result: …….

Tests for effective inactivation (primary test and subcultivation)

Number of doses tested: …….
Volume tested: …….
Type of primary monkey kidney cells: …….
Positive controls: …….
Specification: …….
Dates: …….
Result: …….

3.2.2.4 Concentrated inactivated trivalent bulk (where applicable)

Batch number (s): ……
Date of pooling: ……

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

Residual protein purification marker

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

Test for sterility

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

Result: ……...

D antigen content for each polio type
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

Tests for effective inactivation (primary test and subcultivation)

Number of doses tested: ……..
Volume tested: ……..
Type of primary monkey kidney cells: ……..
Positive controls: ……..
Specification: ……..
Dates: ……..
Result: ……..

3.2.2.5 Final bulk

Batch number: ……..
Date of manufacture: ……..
Volume, storage temperature, storage
time and approved storage period: ……..

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

Total protein content
Method: ……..
Specification: ……..
Date: ……..
Result: ……..

2-phenoxyethanol content
Method: …….
Specification: …….
Date: …….
Result: …….

Free formaldehyde content
Method: …….

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

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

General safety test
Method: …….
Specification: …….
Date: …….
Result: …….

Assay (In vivo potency test)
Species, strain, sex and weight specifications: ……..
Dates of vaccination: ……..
Batch number of reference vaccine: ……..
Vaccine doses (dilutions): ……..
Date of bleeding: ……..
Date of assay: ……..
Number of animals responding at each dose: ……..
ED_{50} of reference and test vaccine:
……..
Potency of test vaccine: ……..
Validity criteria (linearity, parallelism, precision,
ED50 between highest and lowest response): ……..
Results: ……..

D antigen content for each type
Method: ……..
Specification: ……..
Date: ……..
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: …….

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

Assay (*in vivo* assay if not performed on final bulk) or *in vitro* assay (D antigen content)
Method: …….
Specification: …….
Date: …….
Result: …….

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

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

Total protein content
Method: …….
Specification: …….
Date: …….
Result: …….

Free formaldehyde content
Method: …….
Specification: …….
Date: …….
Result: …….

Test for sterility

Method: ……..

Media: ……..

Volume inoculated: ……..

Date test on: ……..

Date test off: ……..

Result: ……..

Bacterial endotoxins

Method: ……

Specification: ……

Date: ……

Result: ……

Preservative content

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 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: _____