FOOD AND DRUGS AUTHORITY GHANA

GUIDELINES FOR BATCH RELEASE OF VACCINES

HEPATITIS B 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:

On the bulk purified antigen:

- Identity
- purity

On the final lot:

- Identity and Assay (the assay serves as an identity test)
- *in vitro* assay used to determine the antigen content must be done on the final lot.
- *in vivo* assay is required only when a new final bulk has been used**.**

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 the tests are required (pass or fail is not sufficient, results of re-test 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 (antigen concentration)/volume of single human dose:…….

Target group (children or adults): …….....

Production cell: …….....

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 and whenever a change has been introduced.

3.2.1.1 Cell banks

Master cell bank (MCB) lot number and 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) lot number: ……..

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: ……..

Production cell lot number: ……..

Identification of cell substrate

Method used: ……..

Nature and concentration of antibiotics or selecting agent (s) 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 Fermentation

Details on production cells (Scaling-up dates): ……..

Date of thawing ampoule of MWCB: ……..

Number of culture flask(s): ……..

Dates of passages: ……..

Incubation times: ……..

Dates of harvesting: ……..

3.2.1.3 Control cell cultures if mammalian cells are used for production

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 (%) of 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: ……...

3.2.2 Intermediate stages

Production details, in-process controls and dates of tests. Identification of intermediates e.g. harvests, bulks, Safety tests on intermediates and controls e.g. sterility, adventitious agents, special tests as antigenicity. Details of storage conditions.

3.2.2.1 Harvests

Report results of tests for each single fermentation lot, using extra pages if necessary.

Batch number(s): …….
Date of inoculation: …….
Date of harvesting: …….

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

Plasmid retention
Method: …….
Specification: …….
Date: …….
Result: …….

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

Mycoplasma (if mammalian cells are used for production) Method:
Media: ……..
Volume inoculated: ……..
Date test on: ……..
Date test off: ……..
Result: ……..

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

Reverse transcriptase assay
Method: ……...
Specification: ……...
Date: ……...
Result: ……...

3.2.2.2 Purified bulk

Batch number(s) of purified bulk: ……..
Date(s) of purification: ……..
Volume(s), storage temperature,
storage time and approved storage period: ……..

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

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

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

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

Protein purity (add PAGE photographs or chromatograms)
Method: ……...
Specification: ……...
Date: ……....
Result: ……....

Residual DNA
Method: ……...

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

Composition (protein, lipid, polysaccharide)
Method: ……...
Specification: ……...
Date: ……...
Result: ……...

Residual chemical(s)
Method: ……...
Specification: ……...
Date: ....……..
Result: ……...

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

Additionally, if mammalian cells and animal serum are used for production the following tests should be carried out:

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

3.2.2.3 Adsorbed bulk vaccine

Report results of tests for each batch of purified bulk used in the composition of the final bulk vaccine, using extra pages if necessary

Batch number(s) of adsorbed bulk vaccine: ……....
Adsorption date: ……...
Volumes, batch number (s) of all components
used during formulation storage temperature,

storage time and approved storage period: ……...

Degree of adsorption
Method: ……...
Specification: ……...
Date: ……...
Result: ……...

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

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

Residual chemical(s)
Method: ……...
Specification: ……...
Date: ……...
Result: ……...

Adjuvant concentration
Method: ……....
Specification: ……....
Date: ……....
Result: ……....

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

pH
Method: ……....
Specification: ……....

Date: ……....
Result: ……....

Freezing point
Method: ……....
Specification: ……....
Date: ……....
Result: ……...

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

In vitro assay (antigen content)
Method: ……....
Batch number of reference vaccine and assigned potency: ……
Date of assay: ……
Validity parameters (linearity, parallelism): ……....
Potency result with 95% fiducial limits: ……....

In vivo assay (where applicable)
Species, strain, sex, and weight specifications: ……....
Date of vaccination: ……....
Date of bleeding: ……....
Date of assay: ……
Batch number of reference vaccine and assigned potency: ……
Vaccine doses (dilutions) and number
of animals responding at each dose: ……....
ED_{50} of reference and test vaccine: ……....
Potency of test vaccine vs. reference vaccine
with 95% fiducial limits: ……
Validity criteria (linearity, parallelism,
precision, ED_{50} between highest and lowest response):
……....

3.2.2.4 Final bulk vaccine
Report results of tests for each batch of adsorbed bulk.

Batch number of final bulk vaccine: ……....

Pooling date: ……....

Volumes, batch number (s) of all components used during formulation, storage temperature, storage time and approved storage time period: ……....

Batch number(s) of adsorbed bulk vaccine: ……....

Volume: ……....

Batch number(s) of bulk alum diluent: ……....

Volume: ……....

Test for sterility

Method: ……....

Media: ……....

Volume inoculated: ……....

Date test on: ……....

Date test off: ……....

Result: ……....

Adjuvant concentration

Method: ……....

Specification: ……....

Date: ……....

Result: ……....

Degree of adsorption (if not performed at previous stages)

Method: ……....

Specification: ……....

Date: ……....

Result: ……....

Preservative content

Method: ……....

Specification: ……....

Date: ……....

Result: ……....

Free formaldehyde content

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: ……....

pH

Method: ……....

Specification: ……....

Date: ……....

Result: ……....

Extractable volume

Method: ……....

Specification: ……....

Date: ……....

Result: ……....

Freezing point

Method: ……....

Specification: ……....

Date: ……....

Result: ……....

Adjuvant concentration
Method: ……....
Specification: ……....
Date: ……....
Result: ……....

Preservative 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: ……....

Test for abnormal toxicity
Method: ……....
Specification: ……....
Observation period: ……....
Number & species of animals: ……....
Date: ……....
Result: ……....

In vitro Assay

Method: ……....
Specification: ……....
Batch number of reference vaccine and assigned potency: …….....
Date of assay: ……
Validity parameters (linearity, parallelism): ……....
Potency result with 95% fiducial limits: ……....

In vivo assay

Species, strain, sex, and weight specifications: ……....
Date of vaccination: ……....
Date of bleeding: ……....
Date of assay: ……
Batch number of reference vaccine and assigned potency: ……
Vaccine doses (dilutions) and number
of animals responding at each dose: ……....
ED_{50} of reference and test vaccine: ……....
Potency of test vaccine vs. reference vaccine
with 95% fiducial limits: ……....
Validity criteria (linearity, parallelism, precision,
ED_{50} between highest and lowest response):
……....

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: _____