FOOD AND DRUGS AUTHORITY GHANA

GUIDELINES FOR BATCH RELEASE OF VACCINES

HEPATITS A (INACTIVATED AND ABSORBED) VACCINE

FDA/SMC/BPU/BR-HAV/2013/06

1 Introduction

These Guidelines outline the minimum Ghana Food and Drugs Authoritybatch 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:

- *in vivo* assay may be done on the final bulk or on a lot of finished product derived from it

- *in vitro* assay to determine the antigen content must be done on the final lot

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 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 final lot of finished product

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 number 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 are a requirement for first submission only.

3.2.1.1 Virus seed lots

Virus strain and reference number used to prepare the hepatitis A vaccine: ……

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

Number of passages between two seeds mentioned above: ……..

Dates of approval of protocol indicating compliance with the requirements of the relevant official monographs and conditions of registration: **……...**

Working seed lot number & preparation date: **……...**

Passage level from Master seed lot

(at most five passage level): ……...

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

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

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

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

Production cell lot number: ……...

Date of thawing ampoule of MWCB: ……

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

Number of culture flasks: …….....

Dates of passages (at most five): …….……...

Incubation time(s): ……...

Identification of cell substrate (Method used): …….....

Nature and concentration of antibiotics used in production 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): …….....

3.2.1.3 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 (specific reasons): ……...
Result: ……

Karyotype

Method: ……
Reference cells: ……...
Date test on: ……...
Date test off: ……...
Result: ……...

Identity test by DNA finger printing (If applicable)

Method: ……..
Probe: ……...
Reference cells: ……..
Restriction enzymes: ……....
Date test on: …. ……
Date test off: ……...
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(s) of simian cells: ……
Quantity of sample inoculated: …….....
Incubation temperature: ……...
Date test on: ……...
Date test off: ……...
Percentage (%) of viable culture at the end: ……...
Result: ……...

Type(s) 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 No 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 used: ……
Volume inoculated: ……...
Date test on: ..……
Date test off: ……
Result: ……...

Test for sterility
Method: ……...
Media used: ……
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: ……...

Test for virus identity

Method: ……..

Specification: ……..

Date test on: ……..

Date test off: ……..

Result: ……..

Virus concentration (infectivity and/or Hepatitis A Virus (HAV) antigenconcentration)

Method: ……..

Reference preparation: ……..

Specification: ……..

Date test on: ……..

Date test off: ……..

Result: ……..

Test for sterility

Method: ……..

Media used: ……..

Volume inoculated: ……..

Date test on: ……..

Date test off: ……..

Result: ……..

Mycoplasma

Method: ……

Media used: ……

Volume inoculated: ……..

Date test on: ……

Date test off: ……

Result: ……..

3.2.2.2 Purified virus harvest:

Batch number (s): ……

Date(s) of purification: ……

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

Report results of tests for each purified virus harvest

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

Virus concentration
Method: …….
Reference preparation: …….
Specification: …….
Date: …….
Result: …….

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

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

Specific activity (Ratio Hepatitis A antigen: total protein)
Method: ……...
Specification: ……...
Date: ……...
Result: ……

Test for residual protein purification marker
Method: ……...
Specification: ……...
Date: ……...
Result: ……

3.2.2.3 Inactivated purified virus harvest

Batch number (s) of inactivated purified virus harvest: ……...

Date(s) of inactivation: ……...

Volume(s), storage temperature, storage time and

approved storage period: ……

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

Tests for effective inactivation
(primary test and sub-cultivation) : ……..
Number of doses tested: ……..
Volume and number of human doses tested: ……..
Type of human diploid cells: ……..
Positive controls with live virus: ……..
Date test on: ……..
Date test off: ……..
Result: ……..

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

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

Purity : ratio Protein/ antigen unit
Method: ……..
Specification: ……..
Date: ……..
Result: ……

Free formaldehyde content
Method: ……

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

3.2.2.4 Final bulk vaccine
Batch number: ……..
Volumes and batch numbers
of all components used during formulation: ……..
Pooling date: ……
Date of manufacture: ……
Volume(s), storage temperature,
storage time and approved storage period: ……..

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

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

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

In vivo assay
Species, strain, sex, and weight specifications: ……
Dates of immunization, bleeding and measure of antibodies: ……..
Batch number of reference vaccine: ……..
Vaccine doses (dilutions): ……
Specification: ……
Date(s) of assay(s): ……
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): ……..

In vitro assay
Method: ……
Specification: ……
Batch number of reference vaccine: ……...
Date: ……...
Result: ……
Validity Criteria: ……

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: ……

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

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

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

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

Test for abnormal toxicity
Method: ……....
Specification: ……
Date test on: ……
Date test off: ……
Result: …..……...

Degree of adsorption (antigen content in the supernatant)
Method: ……
Specification: ……
Date test: ……
Result: ……

Bacterial Endotoxins
Method: ……
Specification: ……
Date: ……
Result: ……

Residual chemicals
Method: ……
Specification: ……
Date: ……
Result: ……

In vivo assay (where applicable) (if not performed on final bulk)

Species, strain, sex, and weight specifications: ……...

Dates of immunization, bleeding and measure of antibodies: ……..…….....

Batch number of reference vaccine: ……...

Vaccine doses (dilutions): ……

Specification: ……

Date(s) of assay(s): ……

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): ..……..…….....

In vitro assay (where applicable)

Method: ……..

Reference preparation: ……..……

Specification: ……..

Validity criteria (linearity, parallelism, precision): ……..

Date test on: ……..

Date test off: ……..

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: _____