

**REPUBLIC OF KENYA**

**MINISTRY OF HEALTH**

**PHARMACY AND POISONS BOARD**

APPLICATION FOR REGISTRATION OF HUMAN VACCINE PRODUCT

*(to be submitted as electronic copy in MS-Word only)*

CONFIDENTIAL

(2022)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Form 1** | | | APPLICATION FOR REGISTRATION OF HUMAN VACCINE PRODUCT | | |
| **To** | | | THE CEO  PPB OFFICES,  LENANA ROAD,  DRUG REGISTRATION DEPARTMENT,  P.O. BOX 27663-00506,  NAIROBI. | | |
| **Application Number** | | |  | | |
| **Date of submission of the dossier** | | |  | | |
| **Name of the 1st Assessor** | |  | | | Signature |
| **Name of the 2nd Assessor** | |  | | | Signature |
| **Date of 1st Assessment** | |  | | | |
| **Date of 2nd Assessment** | |  | | | |
| **CONCLUSION OF THE ASSESSMENT**  **RECOMMENDED** *(no outstanding issues)*  **QUERY RAISED** *(Indicate the sections where query is raised)*  **REJECTED** *(indicate the module(s) that led to the rejection)*  ***(Please delete which does not apply)*** | | | |  | |
| **TYPE OF APPLICATION – HUMAN PRODUCT** | | | | | |
| **MODULE 1: ADMINISTRATIVE INFORMATION** | | | | | |
| **SECTION 1: PARTICULARS OF THE PRODUCT** | | | | | |
| **1.11 Name and address of Applicant** | | | | | |
| **Company name:**  **Address:**  **Country:**  **Telephone:**  **E-Mail:** | | | | | |
| **1.12 Type of Medicinal Product Application ( Tick where appropriate)** | | | | | |
| **New (Innovator)**  **OR**  **Generic( Traditional/Follow on vaccines.** | | | | | |
| *For PPB use only* | | | | | |
| **1.2** | **Trade/Proprietary name (prorietary Product name):** | | | | |
| *For PPB use only* | | | | | |
| **1.3** | **Approved / INN / generic name of the immunogenic substance** | | | | |
| *For PPB use only* | | | | | |
| **1.4** | **Strength of immunogenic substance(s) per unit dosage form of the product and specifications of the immunogenic substance(s), including the reference/ monograph standard for each immunogenic substance(s).** | | | | |
| *For PPB use only* | | | | | |
| **1.5** | **Dosage form** | | | | |
| **1.5.1** | **Pharmaceutical Dosage form of the product:** | | | | |
| **1.5.2** | **Specifications of the Finished Pharmaceutical Product:** | | | | |
| **1.5.3** | **Route(s) of administration (use current list of standard terms - European Pharmacopoeia):** | | | | |
| *For PPB use only* | | | | | |
| **1.6** | **Packing/Pack size of the product:** | | | | |
| **1.6.1** | **Pack size:** | | | | |
| **1.6.2** | **Primary packing materials:** | | | | |
| **1.6.3** | **Secondary packing materials:** | | | | |
| *For PPB use only* | | | | | |
| **1.7** | **Visual Description of the product (Add as many rows as necessary)** | | | | |
| *For PPB use only* | | | | | |

|  |  |  |  |
| --- | --- | --- | --- |
| **1.8** | **1.8 Proposed Shelf life of the product (in months):** | | |
| **1.8.1** | Proposed shelf life (after reconstitution or dilution) (if applicable): | | |
| **1.8.2** | Proposed shelf life (after first opening container): | | |
| **1.8.3** | Proposed storage conditions: | | |
| **1.8.4** | Proposed storage conditions after first opening: | | |
| ***For PPB use only*** | | | |
| **1.9** | **Pharmacotherapeutic group and ATC Code** | | |
| **1.9.1** | **Pharmacotherapeutic group:** | | |
| **1.9.2** | **ATC Code:** | | |
| **1.9.3** | **If no ATC code has been assigned, please indicate if an application for ATC code has been made:** | | |
| **1.9.4** | **Proposed indication(s) for the product:** | | |
| ***For PPB use only*** | | | |
| **1.10** | **Indicate Legal category** | | |
| **1.10.1** | **POM (Prescription only Medicine) unless otherwise, provide justification)** | | |
| ***For PPB use only*** | | | |
| **1.11** | **Country of origin or country of release:** | | |
| ***For PPB use only*** | | | |
| **1.12** | **Product Marketing Authorisation in the country of origin. (Attach certificate of pharmaceutical product from competent regulatory authority) If not registered, state reasons** | | |
| **Authorised**  **Country:**  **Date of authorisation:**  **Proprietary name:**  **Authorisation number:**  **Refused**  **Country: Not applicable**  **Date of refusal (dd-mm-yyyy):**  **Reason for Refusal:** | | | **Withdrawn (by applicant after authorisation)**  **Country:**  **Date of withdrawal (dd-mm-yyyy):**  **Proprietary name:**  **Reason for withdrawal:**  **Suspended/revoked (by competent authority)**  **Country: Not applicable**  **date of suspension/revocation (dd-mm-yyyy):**  **Reason for suspension/revocation:** |
| ***For PPB use only*** | | | |
| **1.12.1** | **Registration status from countries with Stringent Regulatory Authorities (SDRAs) where applicable**  **SDRAs - Documents to be attached:** | | |
| ***For PPB use only*** | | | |
| **1.12.2** | **List of countries in which a similar application has been submitted** | | |
| ***For PPB use only*** | | | |
| **1.12.3** | **Statement on whether an application for the Marketing Authorisation has been previously rejected, withdrawn or repeatedly deferred in the EAC Partner States** | | |
| ***For PPB use only*** | | | |
| **1.12.4** | **Certificates of approval of Drug Substances(s)/ immunogenic s substance(s) Master (DMF) by Stringent Regulatory Authority** | | |
| ***For PPB use only*** | | | |
| **1.12.5** | Manufacturing Licence and Product Licence | | |
| ***For PPB use only*** | | | |
| **1.13** | Certificate of Analysis from a WHO Prequalified Laboratory in Kenya and the  lot release certificate issued by the regulatory authority of country of origin  for those samples submitted with the application | | |
| ***For PPB use only*** | | | |
| **1.14** | Name(s) and complete address (es) of the manufacturer(s) | | |
| **1.14.1** | Name and complete address(es)of the manufacturer(s) of the FPP, including the finished pharmaceutical product release if different from the manufacturer. | | |
| **Marketing Authorisation Holder:**  **Company name:**  **Address:**  **Country:**  **Telephone:**  **E-Mail:**  **Manufactured By:**  **Company) Name:**  **Address:**  **Country:.**  **Telephone:**  **Telefax :**  **If the manufacturer is different to 1.1 above, explain the relationship** | | | |
| 1.14.2 | Name(s) and complete address (es) of the manufacturer(s) of the **active immunogenic substance** | | |
| **The active immunogenic substance: (Add as many rows as necessary)**  **Company) Name:**  **Office Address :**  **Country :**  **Telephone :**  **Fax :**  **Contact Person :**  **E-mail :** | | | |
| ***For PPB use only*** | | | |
| **1.15** | **Compliance to Good Manufacturing Practice (GMP) and Good Clinical Practice** | | |
| **1.15.1** | **Good Manufacturing Practice (GMP) from PPB** | | |
| **1.15.2** | **Good Clinical Practice (GCP) or Good Laboratory Practice (GLP)** | | |
| ***For PPB use only*** | | | |
| **1.16 .1** | **Name and complete address of the Local Technical Representative of Manufacture (for finished pharmaceutical Product)**  **Company name:**  **Address:**  **Country:**  **Telephone:**  **E-Mail:**  **If the Local Technical Representative is different to 1.1 above, explain and provide evidence for the relationship:** | | |
| **1.16 .2** | **Name and address (physical and postal) of the person or company responsible for pharmacovigilance**  **Company name:**  **Address:**  **Country:**  **Telephone:**  **E-Mail:** | | |
| *For PPB use only* | | | |
| **1.17** | **Product Information** | | |
| **1.17.1** | **Summary of Product Characteristics (SPC):** | | |
| **1.17.2** | **Prescribers/Patient information leaflet:** | | |
| **1.17.3** | **Mock-ups and Photo scan of the product:** | | |
| **1.18** | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | 1.18 Batch number(s) and Batch Types of the final product used in | | | | | | | | | | | | | | | Clinical studies | | | | | |  | | | | | | | | | Stability studies | | | | | |  | | |  | |  | | | | Validation/production scale batches | | | | | |  | | |  | |  | | | | Comments:  Comments [e.g., batch size, explanation of NA (not applicable) answers] | | | | | | | | | | | | | | | Quantitative composition (Administration Unit) of the immunogenic substance(s) and excipient(s)  A note should be given as to which quantity the composition refers (e.g. per ml). | | | | | | | | | | | | | | | Ingredients | Administration Unit | | Clinical studies [batch number(s) | | | | Primary stability  [batch number (s) | | | Production  [batch number (s) | | | | | | Quantity /  dosage unit | Unit of measure | | Quantity /  dosage unit | Unit of measure | | Quantity /  dosage unit | Unit of measure | | Quantity /  dosage unit | | | Unit  of  measure | | Active (Name of immunogen(s) | | | | | | | | | | | | | | | 1 |  |  | |  |  | |  |  | |  | |  | | | 2 |  |  | |  |  | |  |  | |  | |  | | | e.t.c |  |  | |  |  | |  |  | |  | |  | | | Name Excipients: | | | | | | | | | | | | | | | 1 |  |  | |  |  | |  |  | |  | |  | | | 2 |  |  | |  |  | |  |  | |  | |  | | | e.t.c |  |  | |  |  | |  |  | |  | |  | | |  |  |  | |  |  | |  |  | |  | |  | | | Note: Only one name for each substance should be given in the following order of priority: INN, Pharmacopoeia, common name, scientific name. | | | | | | | | | | | | | | |  | | | | | | | | | | | | | | | |
| |  |  |  | | --- | --- | --- | | 1.19 | State the reference/monograph standard such as British Pharmacopeia, United States Pharmacopeia, Ph. Eur, Japanese Pharmacopeia, In-house monograph  e.t.c. used for Finished Medicinal Product. | | | 1.20 | | Name and address (physical and postal) of the Contract Research Organisation(s) where the clinical studies of the product were conducted. (If applicable) | | Name: N/A  Company name:  Address:  Country:  Telephone:  Telefax:  E-Mail: | | |  |  |  | | --- | --- | | 1.21 DECLARATION BY AN APPLICANT | | |  | 1. I, the undersigned certify that all the information in this form and accompanying documentation is correct, complete and true to the best of my knowledge. 2. I further confirm that the information referred to in my application dossier is available for verification during GMP inspection. 3. I also agree that I shall carry out pharmacovigelance to monitor the safety of the product in the market and provide safety update reports to the National Medicines Regulatory Authority. 4. I further agree that I am obliged to follow the requirements of Kenya, and 5. Legislations and Regulations which are applicable to medicinal products.   Name:  Position in the company:  Signature:  Date:  Official stamp:……………………………..  *\* Note: If fees have been paid, attach proof of payment* | | | | |
| PPB use only  **OVERALL QUERIES AND RECOMMENDATIONS FOR THIS MODULE** | | | |

**MODULE 2: OVERVIEWS AND SUMMARIES**

Provide a summary of quality (chemical, pharmaceutical, and biological); nonclinical and clinical information presented in modules 3, 4, and 5 in the market authorization application.

* 1. **Table of contents**

Provide a table of contents of the scientific information contained in

modules 2

* 1. **Introduction**

Provide a summary of the type of vaccine, composition, immunological mechanism, and proposed indications for the vaccine .

* 1. **Quality Overall Summary (QOS) - annex III of the Guideline**

Provide a summary of the quality of the product, related to the chemical, pharmaceutical, and biological aspects as presented in module 3 as detailed below :

**2.3. S Immunogenic substance (name, manufacturer)**

**2.3. S.1 General information, starting materials and raw materials**

2.3. S.1.1 Nomenclature

(a) WHO or Pharmacopoeal name(s)

(b) Biological name

(c) For combination vaccines (names of immunogenic substances)

(d) Chemical modification/conjugation of the immunogenic substance

2.3. S.1.2 Structure

(a) Structural formula

(b) Schematic amino acids sequence/molecular formula

(c) Relative molecular mass

2.3.S.1.3 Physicochemical Characterization and Biological Activity

3.2.S.1.3.1 Physicochemical Characterization

3.2.S.1.3.2 Biological Activity

2.3.S.1.4 General description of the starting materials of biological origin used to obtain or extract the immunogenic substance

2.3.S.1.5 General description of the raw materials

2.3.S.1.6 Analytical certificates signed by the manufacturer and the applicant

**2.3. S.2 Manufacture of the immunogenic substance (name,**

**Manufacturer)**

2.3. S.2.1 Manufacturer(s)

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing, and storage) of each manufacturer, including contractors and each proposed production site or facility involved in these activities:

|  |  |
| --- | --- |
| Name and address  (including block(s)/unit(s)) | Responsibility |
|  |  |
|  |  |
|  |  |

(b) Manufacturing authorization for the production of API(s) and, where available, certificate of GMP compliance (GMP information should be provided in *Module 1*):

2.3. S.2.2 Immunogenic substance manufacturing process

(a) Flow diagram of manufacturing process

(b) Narrative description of the manufacturing process (es)

(c) In process holding steps

(d) Description of lot identification system

(e) Description and validation of the inactivation or detoxification process

(f) Description of the purification process

(g) Description of the conjugation process

(h) Stabilization of the immunogenic substance

(i) Reprocessing (if applicable)

(j) Filling Procedure

2.3. S.2.3 Control of critical steps and intermediates

(a) Critical steps in the process and controls performed

(b) Description of sampling procedures

**2.3.S.2.4 Process Validation and/or evaluation**

**2.3. S.3 Characterization of the immunogenic substance**

1. Details of analytical testing
2. Impurities
3. Product related Impurities
4. Process related Impurities

**2.3. S.4 Control of the Immunogenic Substance**

2.3. S.4.1 Specifications

2.3. S.4.2 Description of Analytical Procedures

2.3. S.4.3 Analytical Method validation

2.3. S.4.4 Batch analysis and Production consistency

2.3. S.4.5 Justification of the quality specifications

**2.3. S.5 Reference Standards or Materials (name, manufacturer)**

1. Source (including lot number) of primary reference standards or reference

materials

(e.g.Ph.Int., Ph.Eur., BP, USP, in-house)

(b) Characterization and evaluation of non-official (e.g. not from an officially recognized

pharmacopoeia) primary reference standards or reference materials (e.g. elucidation of structure, certificate of analysis)

(c) Description of the process controls of the secondary reference standard (comparative certificate of analysis and IR spectra against primary standard)

**2.3. S.6 Packaging and container closure system of the immunogenic substance**

**2.3. S.7 Stability of the immunogenic substance**

1. Stability Studies Protocol
2. Stability program or stability commitment
3. Stability data
4. Stability studies conclusion and proposed storage and transportation conditions

**2.3. P FINISHED IMMUNOGENIC PRODUCT (NAME, MANUFACTURER)**

**2.3. P.1 Description and Composition**

(a) Description of the finished immunogenic product

(b) Composition of the finished immunogenic product

| Component and quality standard (and grade, if applicable) | Function | Strength (label claim) | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  | |  | |
| Quant. per unit or per mL | % | Quant. per unit or per mL | % | Quantity per unit or per mL | % |
| <complete with appropriate titles | | | | | | | |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| Subtotal 1 |  |  |  |  |  |  |  |
| <complete with appropriate title | | | | | | | |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| Subtotal 2 |  |  |  |  |  |  |  |
| Total |  |  |  |  |  |  |  |

1. Type of container closure system used for the FPP and accompanying reconstitution diluents, if applicable:

**2.3. P.2 Pharmaceutical Development**

2.3. P.2.1 Compatibility of Immunogenic Substance with other components

2.3. P.2.2 Adjuvant, preservative, stabilizers, and excipients

2.3. P.2.3 Development of the manufacturing process

2.3. P.2.4 Container closure system

**2.3. P.3 Manufacture processes of the finished immunogenic product**

2.3. P.3.1 Manufacturer(s)

1. Name, address and responsibility (e.g. fabrication, packaging, labelling, and testing) of each manufacturer, including contractors and each proposed production site or facility involved in manufacturing and testing:

| Name and address  (include block(s)/unit(s)) | Responsibility |
| --- | --- |
|  |  |
|  |  |
|  |  |
|  |  |

1. Manufacturing authorization, marketing authorization and, where available,

WHO-type certificate of GMP (GMP information should be provided in *Module 1*):

2.3. P.3.2 Batch Formula

Largest intended commercial lot size:

Other intended commercial lot sizes:

(a) List of all components of the finished immunogenic product to be used in the

manufacturing process and their amounts on a per batch basis;

2.3. P.3.3 Description of the manufacturing process

(a) Flow diagram of the manufacturing process

(b) Narrative description of the manufacturing process, including equipment type and working capacity, process parameters:

2.3. P.3.4 Controls of Critical Steps and Intermediates

1. Summary of controls performed at the critical steps of the manufacturing

process and on isolated intermediates:

| Step  (e.g. granulation, compression, coating) | Controls (parameters/limits/frequency of testing) |
| --- | --- |
|  |  |
|  |  |
|  |  |
|  |  |

2.3. P.3.5 Validation and/or evaluation of the processes

2.3. P.3.6 Description of the batch identification system

**2.3. P.4 Control of the adjuvant, preservative, stabilizers, and excipients**

2.3. P.4.1 Specifications

(a) Summary of the specifications

2.3. P.4.2 Analytical Procedures

Summary of the analytical procedures for supplementary tests

2.3. P.4.3 Validation of Analytical Procedures

1. Summary of the validation information for the analytical procedures for supplementary tests (where applicable)

2.3. P.4.4 Justification of Specifications

1. Justification of the specifications (e.g. evolution of tests, analytical

procedures and acceptance criteria, exclusion of certain tests, differences from officially recognized compendial standard(s)):

2.3. P.4.5 Excipients of Human or Animal Origin

1. For FPPs using excipients without risk of transmitting agents of animal spongiform encephalopathies, a letter of attestation confirming this can be found in:

(b) CEP(s) demonstrating TSE-compliance can be found in:

2.3. P.4.6 Novel Excipients

**2.3. P.5 Control of finished immunogenic product**

2.3. P.5.1 Specifications of the immunogenic product

2.3. P.5.2 Analytical Procedures

(a) Summary or references to analytical procedures

2.3. P.5.3 Validation of Analytical Procedures

(a) Summary or references to the validation information

2.3. P.5.4. Lot consistency and analysis

(a) Description of the lots:

| Strength and  batch number | Batch size | Date and  site of production | Use (e.g clinical, comparability studies etc) |
| --- | --- | --- | --- |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

2.3. P.5.5 Characterization and/or determination of impurities

2.3. P.5.6 Justification of Specification(s)

3.2. P.5.7 Analytical certificates

**2.3. P.6 Reference Standards or Materials**

1. Source (including lot number) of primary reference standards or reference

materials (e.g. Ph.Int., Ph.Eur., BP, USP, in-house) *not* discussed in 3.2.S.5:

1. Characterization and evaluation of non-official primary reference
2. Description of the process controls of the secondary reference standard

**2.3. P.7 Container Closure System**

1. Description of the container closure systems, including unit count or fill size,

container size or volume:

|  |  |  |  |
| --- | --- | --- | --- |
| Description  (including materials of construction) | Strength/concentration | Unit count or fill size | Container size  (e.g. 1ml, 2ml, 5ml, etc.) |
|  |  |  |  |
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**2.3. P.8 Stability of the Finished Immunogenic Product**

2.3. P.8.1 Protocols and results of the stability study that justify the proposed validity period.

1. Summary of accelerated and long-term testing parameters (e.g. studies

conducted):

| Storage conditions (◦C, % RH) | Strength and batch number | Batch size | Container closure system | Completed (and proposed) test intervals |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

(b) Proposed storage statement and shelf-life (and in-use storage conditions and in-use period, if applicable):

|  |  |  |
| --- | --- | --- |
| Container closure system | Storage statement | Shelf-life |
|  |  |  |
|  |  |  |

2.3. P.8.2 Post-approval stability program

1. Stability protocol for *Primary stability batches*, Commitment batches and Ongoing batches

2.3. P.8.3 Stability Data

1. The actual stability results should be provided in *Module 3*.
2. Summary of analytical procedures and validation information for those

procedures *not* previously summarized in 2.3.P.5 (e.g. analytical procedures used only for stability studies):

1. Data to support freeze thaw cycles recommended

2.3. P.8.4 Description of the procedures used to guarantee the cold chain

**2.3. A APPENDICES**

3.2.A.1 Facilities and Equipment (name, manufacturer)

3.2.A.2 Adventitious Agents Safety Evaluation (name, dosage form, manufacturer)

3.2.A.3 Excipients

3.2. R: Summary lot protocols

**2. 4 Overview and summary of the nonclinical studies**

Provide an overview and summary of the results of the pharmacological, pharmacokinetic, and toxicological tests on animals and/or *in vitro* studies done as presented in Module 4: Provide the information as a written and tabulated summary, in the following order:

1. Introduction
2. Written pharmacological summary
3. Tabulated pharmacological summary
4. Written pharmacokinetic summary (when appropriate)

Tabulated pharmacokinetic summary (when appropriate)

1. Written toxicological summar
2. Tabulated toxicological summary

**2. 5 Overview and summary of the clinical studies**

Provide a critical analysis of the clinical results included in the clinical summary and in module 5. The Information should include a summary of the clinical development of the product, the design of the pivotal studies, and the decisions related to the clinical studies and their performance and it should include an overview of the clinical conclusions and an evaluation of the risks/benefits in relation to the results of the clinical studies and justification of the proposed dosages. All the data related to efficacy/effectiveness and safety assessed through the development of the product should be summarized in this section as well as any study limitations. Summaries should include of all the clinical studies performed and synopsis of each study.

The data should be presented in a written and tabulated summary in the following order:

1. Introduction
2. Detailed discussion of the development of the product
3. Overview of immunogenicity
4. Overview of the efficacy
5. Overview of the safety
6. Conclusions and risk/benefit analysis
7. Bibliography