



**Title: GUIDELINES FOR
THE REGISTRATION OF
VACCINES**



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

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Start of public Consultation	
End of public Consultation	
Agreed by QMS committee	
Approved by Board	

**Pharmacy Board of Sierra Leone,
PMB 322
Central Medical Stores Compound
New England Ville
Freetown**



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Contents

ACKNOWLEDGEMENTS	4
EXECUTIVE SUMMARY	4
1.0 INTRODUCTION	4
2.0 OBJECTIVE.....	5
4.0 GLOSSARY	6
MODULE 1: ADMINISTRATIVE - LEGAL INFORMATION	10
MODULE 2: SUMMARIES/OVERVIEWS.....	12
MODULE 3: QUALITY INFORMATION (CHEMISTRY, MANUFACTURE AND CONTROL)	13
MODULE 4.....	18
MODULE 5.....	19
CHAPTER 2	20
GUIDELINES FOR THE PREPARATION OF THE APPLICATION	20
INTRODUCTION	20
MODULE 1.....	21
ADMINISTRATIVE - LEGAL INFORMATION	21
1.3 SUMMARY OF PRODUCT CHARACTERISTICS AND PRODUCT LABELING	24
1.4 LIST OF COUNTRIES WHERE THE PRODUCT HAS BEEN LICENSED AND SUMMARY OF APPROVAL CONDITIONS.....	29
2.1 GENERAL TABLE OF CONTENTS.....	30

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

MODULE 3	33
QUALITY INFORMATION (CHEMISTRY, MANUFACTURE AND CONTROL)	33
3.1 TABLE OF CONTENTS OF MODULE 3	33
MODULE 4	44
MODULE 5	46
CLINICAL INFORMATION	46
GENERAL COMMENTS	46
7.0 APPENDICES	50
APPENDIX I	50
RISK MANAGEMENT PLAN (RMP).....	51
SANCTIONS AND PENALTIES	54
RELEVANT INFORMATION TO BE INCLUDED IN DOSSIER	55
APPENDIX V:	58
RELEVANT PBSL GUIDANCE DOCUMENTS.....	58
APPENDIX VI:	59
APPENDIX VII:	59
ABBREVIATIONS AND ACRONYMS	59



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar



ACKNOWLEDGEMENTS

EXECUTIVE SUMMARY

1.0 INTRODUCTION

The responsibility for the quality, safety and efficacy of vaccines lies first and foremost with the manufacturer. The Pharmacy Board of Sierra Leone (PBSL) guidelines for the registration of vaccines provide the requirement for registration applications to ensure that products and manufacturers meet the established regulatory criteria.

Vaccines are products of biological origin which exhibit some intrinsic variability. They are characterized by complex manufacturing processes and are administered to large numbers of healthy children, adolescents and adults. Their quality cannot be assessed solely by testing the final product alone.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

The PBSL evaluates the quality, efficacy and safety of all vaccines intended to be imported, retailed and use in Sierra Leone. The PBSL shall register the vaccine and grant marketing authorization following satisfactory evaluation outcome.

The PBSL guidelines gives information needed in the application dossier, and evidence that the vaccine has passed the stages of research, development, production and quality control, as well as clinical testing, and guarantees that the quality, safety and efficacy required of the vaccine to be used in humans has been established.



Another important aspect to consider in the vaccine evaluation process is that the manufacturing facilities must comply with current Good Manufacturing Practices (cGMP).

2.0 OBJECTIVE

This revised guideline presents a common format for the preparation of an application that will be submitted to the Pharmacy Board of Sierra Leone (PBSL).

This revised guideline has been improved to assist in the following;

- Preparation of documentation for pharmaceutical products by providing clear guidance on the format.
- Fully adopt the modular format of the Common Technical Document (CTD) as developed by International Conference on Harmonization (ICH) as well as World Health Organization (WHO) Guidelines on Submission of Documentation for Prequalification of Vaccines and other Biological Products.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar



- Provide guidance on the technical and other general data requirements.
- Reduce the time lines to compile applications for registration of Vaccines and other Biological Products.
- Give more details on the requirements for active ingredients as well as finished product (FP).
- Promote effective and efficient processes for the development of these applications and the subsequent evaluation processes by the PBSL.

Through the ICH process, considerable harmonization has been achieved on the organization of registration documents with the issuance of the CTD. This harmonized format has become widely accepted by regulatory authorities both within and beyond the ICH Regions.

3.0 SCOPE



The PBSL guidance document applies to all registration application for vaccines intended for use in humans, regardless of where they were manufactured, whether they are licensed in the country of origin or not. The guidance document consisted of five modules (i.e. Module 1- Module 5) and it is in Common Technical Document format.

4.0 GLOSSARY

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

The definitions herein apply to the harmonized requirements for the registration applications of vaccines and its guideline for preparation of application are included in this glossary in alphabetical order.

- Active ingredient of the vaccine: the antigenic substances (or compounds thereof) that can induce specific responses in humans against an infectious agent, its antigens or toxins.
- Batch or lot: set of final packages of finished vaccine, hermetically sealed, that is homogeneous with respect to the risk of cross-contamination during the packing and freeze-drying processes.
- Therefore, all final packages must have been filled from a single set of ingredients in a single working session and, if applicable, freeze-dried in standardized conditions in the same room.
- Carrier protein: a protein used mainly in conjugated polysaccharide vaccines to which the polysaccharide antigen is linked in order to improve both the magnitude and type of the immune response.
- Country of origin: it corresponds to the country where the legal certifications of the product are generated, where is the legal or titular representative and can or not agree with the country where the vaccine makes.
- Dosage form: the physical form in which a product is prepared for administration to the recipient.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Shelf life: it is the date before which the quality of the vaccine remains acceptable for its intended use as outlined in the market authorization. It is established based on stability studies.
- Final bulk product: any product that has gone through all stages of processing, including formulation but not final packaging.
- Finished product: final pharmaceutical form that has gone through all steps of the manufacturing process, including final packaging.
- Good Manufacturing Practices (GMP): set of procedures and practices to ensure consistent controlled production of batches of pharmaceutical products, according to proper quality standards for the intended use thereof and the conditions required for their sale.
- Lot release: process for the evaluation of each individual lot of vaccine submitted to be used in the market; this means independent control of each lot to guarantee that all the lots produced and used in a country are in compliance with the established quality specifications. This process can be performed by detailed review of Summary Protocols of Production and Quality Control, and includes laboratory testing when it is considered necessary.
- License: in some countries it is called registration. Procedure whereby the National Regulatory Authority grants permission for the product in question to be sold and distributed in the country.
- Master cell bank: culture of specific cells of known origin that are distributed in a container or packages in a single operation to ensure uniformity and stability in



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03



**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

storage. The master bank is usually kept at a temperature of -70°C or less. In some countries, it is called the primary bank.

- Product development: all studies to show that the dose, formulation, manufacturing process and packaging system, as well as the microbiological properties, are appropriate for the proposed purpose.
- Product to be licensed: both, the document outlining the harmonized requirements for the licensing of vaccines in the Americas and its guidelines for preparation of application, apply to the registration of vaccines in the Americas. The vaccine may be also referred as the product.
- Raw materials: any substance used to make or extract the active ingredient but from which the active ingredient is not directly derived. For example, culture media, fetal bovine serum, etc.
- Starting materials: any substance of biological origin, such as microorganisms, organs and tissues of plant or animal origin, including cells or fluids of human or animal origin and recombinant cell substrates.
- Validation: series of documented procedures or actions, consistent with good manufacturing practices, demonstrating that the processes, equipment, materials, activities and/or systems satisfy the predetermined specifications and quality attributes.
- Working cell bank: culture of cells derived from a master cell bank and intended to prepare production cultures. The working cell bank is usually kept at a temperature of -70°C or less. In some countries, it is called the secondary bank.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

5.0 SPECIFIC REQUIREMENT

MODULE 1: ADMINISTRATIVE - LEGAL INFORMATION

- 1.1 TABLE OF CONTENTS (MODULES 1 TO 5)
- 1.2 APPLICATION FORM
 - 1.2.1 Proprietary, commercial or trade name of vaccine
 - 1.2.2 Non-proprietary name or common name of vaccine
 - 1.2.3 Concentration
 - 1.2.4 Dosage Form
 - 1.2.5 Senior Executive Officer / Senior Medical or Scientific Officer
 - 1.2.6 Legal Representative in Country
 - 1.2.7 Vaccine proprietary
 - 1.2.8 Manufacturer of active ingredient(s)
 - 1.2.9 Manufacturer of the finished product
 - 1.2.10 Other manufacturers involved in the production process
 - 1.2.11 Officials responsible for releasing batches of finished product
 - 1.2.12 Commercial presentation of vaccine
 - 1.2.13 Route of administration
 - 1.2.14 Storage conditions
 - 1.2.16 Strength of each unit of dose
 - 1.2.16 Legal documents on the product:



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

- Document recognizing the technical director or technical professional responsible for the product
- Authorization of representative
- Certificate of Pharmaceutical Product (CPP)
- Certificate of Good Manufacturing Practices (GMP)
- Trademark certificate (optional)
- Patent certificate (under national legislation)
- Batch release certificate issued by NRA (imported products)
- Manufacturer's statement that all relevant information has been included and is accurate

1.3 SUMMARY OF PRODUCT CHARACTERISTICS AND PRODUCT LABELING

1.3.1 Summary of product characteristics

1.3.2 Product Labeling

1.3.2.1 Primary package label

1.3.2.2 Secondary packaged label

1.3.2.3 Package insert

1.3.2.4 Final packaging

1.3.2.5 Monograph for health professionals or information for prescription in extended or reduced form

1.3.3 Samples

1.3.3.1 Samples of finished product (in accordance with PBSL samples schedule)

1.3.3.2 Summary protocol of batch production and control



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

1.4 LIST OF COUNTRIES WHERE THE PRODUCT HAS BEEN LICENSED AND
SUMMARY OF APPROVAL CONDITIONS

1.5 INFORMATION REGARDING EXPERTS

1.6 ENVIRONMENTAL RISK ASSESSMENT

MODULE 2: SUMMARIES/OVERVIEWS

2.1 GENERAL TABLE OF CONTENTS

2.2 INTRODUCTION

2.3 OVERALL QUALITY SUMMARY

Introduction

2.3. S Summary of Active Biological Substance

2.3. P Summary of finished product

2.4 OVERVIEW OF NON-CLINICAL STUDIES

2.5 OVERVIEW OF CLINICAL STUDIES

Introduction

Table of contents

2.5.1 Detailed discussion of product development

2.5.2 Overview of immunogenicity

2.5.4 Overview of efficacy

2.5.5 Overview of safety

2.5.6 Conclusions on risk-benefit balance



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

2.5.7 Literature References

2.6 NON-CLINICAL SUMMARY

2.6.1 Introduction

2.6.2 Written pharmacological summary

2.6.3 Tabulated pharmacological summary

2.6.4 Written pharmacokinetic summary (when appropriate)

2.6.5 Tabulated pharmacokinetic summary (when appropriate)

2.6.6 Written toxicological summary

2.6.7 Tabulated toxicological summary

2.7 CLINICAL SUMMARY

2.7.1 Introduction

Table of contents

2.7.2 Summary of the clinical immunogenicity studies

2.7.3 Summary of the clinical efficacy studies

2.7.4 Summary of the clinical safety studies

2.7.5 Literature Reference

MODULE 3: QUALITY INFORMATION (CHEMISTRY, MANUFACTURE AND CONTROL)

3.1 TABLE OF CONTENTS OF MODULE 3

3.2 CONTENTS

3.2.S ACTIVE INGREDIENT(S)



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

3.2.S.1 GENERAL INFORMATION STARTING MATERIALS AND RAW MATERIALS

3.2.S.1.1 Trade and/or non-proprietary name(s) of active(s) ingredient(s)

3.2.S.1.2 Structural formula, molecular formula and relative molecular weight (if applicable)

3.2.S.1.3 Description and characterization of active ingredient

3.2.S.1.4 General description of the starting materials

- Strain
- Master / Working Seed System Banks
- Embryonated eggs

3.2.S.1.5 General description of the raw materials

3.2.S.1.6 Analytical certificates signed by the manufacturer and the applicant for licensing

3.2.S.2 MANUFACTURING PROCESS FOR THE ACTIVE INGREDIENT

3.2.S.2.1 Manufacturer(s)

3.2.S.2.2 Description of manufacturing process

- active ingredient, in-process controls

3.2.S.2.3 Material controls

3.2.S.2.4 Identification of critical steps in process and controls. Selection and justification of critical steps

3.2.S.2.5 Validation of manufacturing process. Description of changes



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

3.2.S.3 CHARACTERIZATION OF ACTIVE INGREDIENT

3.2.S.4 QUALITY CONTROL OF ACTIVE INGREDIENT

3.2.S.4.1 Specifications

3.2.S.4.2 Description of analytical procedures, validation and justification of specifications

3.2.S.4.3 Validation of analytical procedures

3.2.S.4.4 Batch analysis and consistency results

3.2.S.4.5 Justification of specifications

3.2.S.5 REFERENCE STANDARDS OR MATERIALS

3.2.S.6 PACKAGING/CONTAINER CLOSURE SYSTEM

3.2.S.7 STABILITY OF ACTIVE INGREDIENT

3.2.S.7.1 Protocol of stability study, summary and conclusions

3.2.S.7.2 Post-approval stability program

3.2.S.7.3 Stability data

3.2.S.7.4 Storage and shipping conditions of active ingredient

3.2.S.8 CONSISTENCY OF PRODUCTION OF ACTIVE
BIOLOGICAL SUBSTANCE

3.2.P FINISHED PRODUCT

3.2.P.1 DESCRIPTION AND COMPOSITION OF FINISHED PRODUCT

3.2.P.2 PHARMACEUTICAL DEVELOPMENT

3.2.P.2.1 Active ingredient

3.2.P.2.2 Finished product



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

3.2.P.2.3 Manufacturing process

3.2.P.2.4 Packaging/container closure system, compatibility

3.2.P.2.7 Justification of final qualitative/quantitative formula

3.2.P.3 MANUFACTURE OF FINISHED PRODUCT

3.2.P.3.1 Manufacturer

3.2.P.3.2 Batch formula

3.2.P.3.3 Description of manufacturing process

3.2.P.3.4 Control of critical and intermediate steps

3.2.P.3.5 Validation and/or evaluation process

3.2.P.3.6 Description of batch identification system

3.2.P.4 CONTROL OF ADJUVANT, PRESERVATIVE, STABILIZERS
AND EXCIPIENTS

3.2.P.4.1 Specifications

3.2.P.4.2 Analytical procedures

3.2.P.4.3 Validation of analytical procedures

3.2.P.4.4 Justification of specifications

3.2.P.4.5 Substances of human or animal origin

3.2.P.4.6 Use of new adjuvant, preservatives, stabilizers and excipients

3.2.P.5 CONTROL OF FINISHED PRODUCT

3.2.P.5.1 Specifications

3.2.P.5.2 Analytical procedures

3.2.P.5.3 Validation of analytical procedures



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

3.2.P.5.4 Batch analysis and consistency results

3.2.P.5.5 Determination and characterization of impurities

3.2.P.5.6 Justification of specifications

3.2.P.5.7 Analytical certificates signed by manufacturer and applicant for licensing

3.2.P.6 REFERENCE STANDARDS OR MATERIALS

3.2.P.7 PACKAGING/CONTAINER CLOSURE SYSTEM

- Specifications of primary and secondary packaging
- Test and evaluation of packaging materials

3.2.P.8 STABILITY

3.2.P.8.1 Protocol of stability study, summary and conclusions:

- For freeze-dried products, include stability study of freeze-dried material, diluents and reconstituted product
- Thermostability (where applicable)

3.2.P.8.2 Post-approval stability program

3.2.P.8.3 Stability data

3.2.P.8.4 Description of procedures to guarantee cold chain



3.2.A APPENDIX

Include the following information in the appendix of Module3:

3.2.A.1 Equipment and facilities

3.2.A.2 Safety evaluation of adventitious agents

3.3 LITERATURE REFERENCES

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

MODULE 4

NON CLINICAL INFORMATION

The non-clinical studies should follow the guidelines of the WHO Guide on non-clinical evaluation of vaccines, Technical Report Series No. 927, WHO, 2005, or the current edition thereof.

4.1 TABLE OF CONTENTS OF MODULE 4

4.2 REPORT ON STUDIES

4.2.1 PHARMACOLOGY

4.2.1.1 Pharmacodynamic studies (immunogenicity of the vaccine)

4.2.1.2 Pharmacodynamic studies of adjuvant (if applicable)

4.2.2 PHARMACOKINETICS

4.2.2.1 Pharmacokinetics studies

4.2.3 TOXICOLOGY

4.2.3.1 General toxicology - information on:

- ☐ Design of study and justification of animal model
- ☐ Animal species used, age and size of groups
- ☐ Dose, route of administration and control groups
- ☐ Parameters monitored
- ☐ Local tolerance

4.2.3.2 Special toxicology (for vaccines to which it applies):

- ☐ Special immunological investigation



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

- ☐ Toxicity studies in special populations
- ☐ Genotoxicity and carcinogenicity studies
- ☐ Reproductive toxicity studies

4.2.3.3 Toxicity of new substances used in formulation (new adjuvant, stabilizers, and additives)

4.2.4 SPECIAL CONSIDERATIONS

4.2.4.1 For attenuated vaccines an evaluation of possibility of microorganism shedding through natural avenues of excretion

4.3 LITERATURE REFERENCES

MODULE 5

CLINICAL INFORMATION



The information should be consistent with the WHO Guidelines on Clinical Evaluation of Vaccines: Regulatory Expectations (WHO Technical Report Series, 924, 2005, or latest edition)

and regulatory guidelines in each country.

5.1 TABLE OF CONTENTS FOR MODULE

5.2 CONTENTS: REPORTS OF CLINICAL STUDIES

- ☐ Phase I studies
- ☐ Phase II studies
- ☐ Phase III studies

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- ☐ Special considerations
- ☐ Adjuvant
- ☐ Non-inferiority studies (for combined vaccines, or approved vaccines prepared by new manufacturers)
- ☐ Combined vaccines or vaccines made by new manufacturers

- 5.3 CLINICAL STUDY REPORTS
- 5.3.6 PHASE IV STUDIES AND/OR PHARMACOVIGILANCE PLAN (IF APPLICABLE)
- 5.4 LITERATURE REFERENCES



CHAPTER 2

GUIDELINES FOR THE PREPARATION OF THE APPLICATION

INTRODUCTION

This document is intended to provide additional guidance to the applicant for the preparation of submissions in Chapter 1 of this document, and also to offer complementary information.

Because of their special characteristics, vaccines are mostly considered as new products for licensing purposes. Vaccines may also be considered as follow-on-biologics or Biosimilars.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

MODULE 1

ADMINISTRATIVE - LEGAL INFORMATION

The requirements include:

1.1 TABLE OF CONTENTS (MODULES 1 TO 5).

The application to license vaccines should include an index of the information contained in each module.

1.2 APPLICATION FORM

PBSL minimum requirement:

- 1.2.1 Proprietary, commercial or trade name of vaccine. It corresponds to the name under which the vaccine will be registered.
- 1.2.2 Non-proprietary name or common name of vaccine. The name adopted by the World Health Organization, the common international name, or the name contained in official pharmacopeias recognized in the country.
- 1.2.3 Concentration. State the concentration of the active ingredient(s) contained in the vaccine.
- 1.2.4 Dosage Form. Indicate the dosage form of the vaccine, for example, injectable solution, and lyophilized power for injectable suspension.
- 1.2.5 Senior Executive Officer / Senior Medical or Scientific Officer. The professional responsible for the product in the country where licensing is applied for. Give the full name, address, telephone, fax, e- mail, professional license number, and the registration number of his/her degree, as per the country's legislation.



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

1.2.6 Legal Representative in Country. Refers to the company that represents the product, which will be responsible for marketing it in the country. Give the full name, address telephone, fax, and e-mail. Some countries in the Region do not require legal representatives resident in the country to obtain the licensing of a product.

1.2.7 Vaccine proprietary. Give the full name of the market authorization holder of the vaccine if licensed in the country of origin, also address, telephone, fax, and e-mail.



1.2.8 Manufacturer of active ingredient(s). Give the name, address, telephone, fax, and e-mail of the manufacturer(s) involved in the production of the active ingredient(s) in the vaccine.

1.2.9 Manufacturer of the finished product. Give the name, address, telephone, fax, and e-mail of the manufacturer(s) involved in the production of the finished product.

1.2.10 Other manufacturer(s) involved in the production process of the vaccines. In the event that some parts of the manufacturing process are performed by a different company, give name, address, telephone, fax, and e-mail. For lyophilized vaccines, include the name, address, telephone, fax, and e-mail of the producer of the diluents.

1.2.11 Official responsible for batch release of finished product. Give the name and position of the person responsible for the release of the lots of vaccine.

1.2.12 Commercial presentation of vaccine. Indicate whether the vaccine is offered for sale in single or multiple doses presentation and whether it will be distributed in a single package or in a multiunit package and whether it contains any additional accessories, for example a transfer device.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar



1.2.13 Route of administration. Indicate the route of administration of the vaccine.

1.2.14 Storage conditions. Indicate the storage temperature for the vaccine and any other storage conditions, for example: protect from light, do not freeze.

1.2.15 Strength of each unit of dose.

1.2.16 Legal documents on the product. The legal information should be duly certified, authenticated under the procedure in effect in the country of origin, and issued by the appropriate entity. The certified documents may be presented during the license process and they will not constitute a limitation for the dossier submission.



- ❖ Document recognizing the technical director or technical professional responsible for the product required based on country's legislation. Submit a document issued by the manufacturer of the vaccine giving information regarding the individuals responsible for the product in the country indicating who is authorized to perform the related regulatory activities, including application for the vaccine licensing.
- ❖ Authorization of representative: Document issued by the manufacturer of the vaccine authorizing the company to represent it and market the vaccine in the country.
- ❖ Certificate of Pharmaceutical Product (CPP). Using WHO model. Required for imported vaccines since it is the certificate issued by the regulatory authority that grants the license in the country of origin. This certificate includes information on compliance with GMP. Some countries issue a Free Sales Certificate (FSC); this should be submitted in addition to the GMP certificate.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

❖ Certificate of Good Manufacturing Practices of all manufacturer(s) involved in the vaccine production process. This should include manufacturers that are involved in any stage of the production process, for example manufacturer(s) of the active ingredient(s), the diluents, and those responsible for labeling packaging the finished product. It is important that the certificate indicates the procedures that the establishment is authorized to perform.

- Trademark certificate (optional)
- Patent certificate (under national legislation)
- Batch release certificate issued by NRA (imported product). Refers to the lot release certificate issued by the regulatory authority of the country of origin of the product or the regional regulatory authority responsible for its release. The certificate should correspond to those samples submitted with the application for licensing, as applicable.
- Manufacturer's statement that all relevant information has been included and is accurate. A document should be presented certifying that the information provided is the information corresponding to all the studies performed, regardless of their results. These include all the pertinent information regarding all toxicological and/or clinical tests or trials of the vaccine that are incomplete or have been abandoned and/or completed tests related to indications not covered by the application.

1.3 SUMMARY OF PRODUCT CHARACTERISTICS AND PRODUCT LABELING



	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

1.3.1 Summary of product characteristics. A summary should be submitted of the characteristics of the vaccine under evaluation.

1.3.2 Product labeling. The text proposed for the primary label, the secondary label or exterior packaging, and the package insert should be included.



1.3.2.1 Primary package label. Submit the label proposed for the vaccine's primary package or container, which should provide the following information as a minimum:

- Proprietary, commercial or trade name
- Non-proprietary name or common name
- Dosage form
- Concentration, potency, or viral titer
- Content/volume
- Volume/dose
- Number of doses per vial (for multidose presentations)
- Route of administration
- Storage temperature (if the size of the package so permits)
- Warnings
- Lot number
- Expiry date
- Manufacturer
- Registration number

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

1.3.2.2 Secondary packaged label. Include the text proposed for the vaccine's secondary packaging, also known as the packaging that protects the primary vaccine container, which should provide the following information as a minimum:



- Proprietary, commercial or trade name
- Non-proprietary name or common name
- Dosage form
- Concentration, potency, or viral titer
- Content/Volume
- Volume/dose
- Number of doses per vial (for multidose presentations)
- Composition
- Excipients
- Product storage
- Route of administration
- Instructions for preparation
- Mode of use
- Warnings
- Identification marks (some countries require that an identification mark indicating the type of product be included, for example a yellow band for pediatric products)
- Lot number
- Date of expiry

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Name and address of the manufacturer of the finished product
- Name and address of the company responsible for packaging
- Name and address of the owner, representative, or distributor
- Name of the professional in charge
- Registration number

1.3.2.3 Package insert. Include the text proposed for the package insert, which should contain the following information as a minimum:

- Proprietary, commercial or trade name
- Non-proprietary or common name
- Pharmaceutical form
- Concentration, potency, or viral titer
- Content/Volume
- Volume/dose
- Number of doses per vial (for multidose presentations)
- Composition
- Excipients
- Cell substrate
- Route of administration
- Indications
- Immunization plan
- Proper use

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Precautions
- Warnings
- Adverse events allegedly associated with vaccination and immunization
- Contraindications
- Use during pregnancy and breast feeding
- Storage of the product/storage conditions
- Name and address of the manufacturer of the finished product
- Name and address of the company responsible for packaging

1.3.2.4 Final packaging. Samples, or alternatively labels and cartons, of the primary and secondary packaging of the vaccine, including the package insert and accessories should be submitted. The purpose of this is to provide an example of the vaccine, including accessories, if any, to verify that they correspond to what is described for the characteristics of the vaccine under evaluation.

1.3.2.5 Monograph for health professionals or information for prescription in extended or reduced form. Submit the proposed monograph on the vaccine to be distributed to health professionals.

1.3.3 Samples

1.3.3.1 Samples of finished product (in accordance with legislation of each country). Samples must be sent for the corresponding analytical evaluation.

1.3.3.2 Summary protocol of batch production and control. This protocol should follow the format recommended by the WHO in the specific requirements for the production and control of the specific vaccine submitted for market authorization. These protocols



**Title: GUIDELINES FOR
THE REGISTRATION OF
VACCINES**



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

are published in the WHO's Technical Report Series. For novel vaccines for which there are no specific WHO recommendations, submit a template of the protocol proposed for its evaluation or a protocol that has been approved by the regulatory authority of the country of origin.

1.4 LIST OF COUNTRIES WHERE THE PRODUCT HAS BEEN LICENSED AND SUMMARY OF APPROVAL CONDITIONS.



The list of countries where the vaccine is registered at the time the application for registration is submitted or, if there are none, the countries where registration is being processed. In the event the product has been registered in other countries, attach the summary of the conditions under which the market authorization was granted by that regulatory authority.

1.5 INFORMATION REGARDING EXPERTS.

A declaration should be sent signed by each of the experts who performed the product evaluation from the standpoint of quality, nonclinical studies and clinical studies. Attach a summary of their academic records and employment experience and state the professional relationship between the experts and the applicant of market authorization.

1.6 ENVIRONMENTAL RISK ASSESSMENT.

Include an evaluation of the possible environmental risks posed by the use and/or disposal of the vaccine and give proposals in that regard and the indications or warnings to be included on the product label.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

MODULE 2: SUMMARIES

The purpose of this module is to summarize the quality (chemical, pharmaceutical, biological); nonclinical and clinical information presented in modules 3, 4, and 5 in the market authorization application. The experts who draft these summaries should take an objective approach to the decisive points related to the quality of the vaccine, clinical and nonclinical studies performed, report all pertinent data for the evaluation, and refer to the corresponding tables included in modules 3, 4, and 5. The information in module 2 should be presented in the following order:

2.1 GENERAL TABLE OF CONTENTS.

A general index should be included of the scientific information contained in modules 2 to 5.

2.2 INTRODUCTION.



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

2.3 OVERALL QUALITY SUMMARY.

A general summary of the quality of the vaccine should be presented, related to the chemical, pharmaceutical, and biological aspects. This summary should refer exclusively to the information, data, and justifications included in module 3 or in other modules of the registration document. The format to be followed is:

INTRODUCTION

2.3.S Summary of active ingredient

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

2.3.P Summary of final product

2.4 OVERVIEW OF NON-CLINICAL STUDIES

A comprehensive and critical assessment of the results of the evaluation of the vaccine in animals and in vitro testing should be presented and the safety characteristics of the vaccine for use in humans should be defined. The data should be presented as a written and tabulated summary, in the following order:

- Introduction
- Written pharmacological summary
- Tabulated pharmacological summary
- Written pharmacokinetic summary (when appropriate)
- Tabulated pharmacokinetic summary (when appropriate)
- Written toxicological summary
- Tabulated toxicological summary

2.5 OVERVIEW OF CLINICAL STUDIES.

Should present a critical analysis of the clinical results included in the clinical summary and in module 5. Include a summary of the clinical development of the vaccine, the design of the pivotal studies, and the decisions related to the clinical studies and their performance, and also an overview of the clinical conclusions and an evaluation of the risks/benefit in relation to the results of the clinical studies and justification of proposed doses should be included. All the data related to efficacy and safety assessed through the development of the vaccine will be presented, as well as any outstanding



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

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

INTRODUCTION

TABLE OF CONTENTS

- 2.5.1 Detailed discussion of product development
- 2.5.2 Overview of immunogenicity
- 2.5.4 Overview of efficacy
- 2.5.5 Overview of safety
- 2.5.6 Conclusions on risk-benefit balance
- 2.5.7 Literature References

2.6 NON-CLINICAL SUMMARY.

A summary of the results of the pharmacological, pharmacokinetic, and toxicological tests on animals and/or "in vitro" should be included. An objective written and tabulated summary should be presented in the following order:

- 2.6.1 Introduction
- 2.6.2 Written pharmacological summary
- 2.6.3 Tabulated pharmacological summary
- 2.6.4 Written pharmacokinetic summary (when appropriate)
- 2.6.5 Tabulated pharmacokinetic summary (when appropriate)
- 2.6.6 Written toxicological summary
- 2.6.7 Tabulated toxicological summary

2.7 CLINICAL SUMMARY.



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

A critical summary of the results submitted in module 5. This summary should include of all the clinical studies performed. It should also present a synopsis of each study. The summary of clinical information should be in the following order:

INTRODUCTION

TABLE OF CONTENTS

- 2.7.2 Summary of the clinical immunogenicity studies
- 2.7.3 Summary of the clinical efficacy studies
- 2.7.4 Summary of the clinical safety studies
- 2.7.5 Literature References

MODULE 3



QUALITY INFORMATION (CHEMISTRY, MANUFACTURE AND CONTROL)

3.1 TABLE OF CONTENTS OF MODULE 3

In accordance with the general plan agreed internationally for registration of vaccines.

3.2 CONTENTS

Corresponds to the basic principles and requirements of the active ingredient(s) and finished product. This includes the chemical, pharmaceutical, biological data on development, the manufacturing process, certificates of analysis, characterization and properties, quality control, specifications and stability of each of the active ingredients and finished product as indicated below.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

3.2. S ACTIVE BIOLOGICAL SUBSTANCE.

The information requested under this point should be supplied individually for each antigen in the vaccine.

3.2. S.1 G E N E R A L INFORMATION, STARTING MATERIALS AND RAW MATERIALS

3.2. S.1.1 T r a d e and/or non-proprietary name(s) of active(s) ingredient(s). Based on the WHO or Pharmacopoeia requirements, as appropriate.

3.2.S.1.2 Structural formula, molecular formula and relative molecular weight (if applicable). For example, in synthetic vaccines containing polysaccharides or proteins include the schematic amino acid sequence, indicating the glycosylation sites or other modifications and relative molecular mass.

3.2. S.1.3 Description and characterization of active ingredient. Including physicochemical properties and biological activity.

3.2. S.1.4

- General description of the starting materials. For each biological starting material used to obtain or extract the active ingredient, include a summary of viral safety of the material:
- Strain: Information on the origin, number of passes, identification, analysis certificates processes of attenuation, development or construction and genetic stability, depending on the type of vaccine strain.



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

- Master/Working/Seed Banks Systems. Origin, identification, characterization, preparation method, analysis certificates, determination of foreign agents, stability, controls, and frequency of the tests, definition of the number of passes. In the case of cell banks, demonstrate that the characteristics of the cells remain unaltered in the passes used in production and successively.
- Embryonated eggs. Information on their origin, identification, quality certificates.

3.2. S.1.5 General description of the raw materials.



Considering the raw materials used in the preparation process from which the active ingredient is not directly derived, such as culture media, bovine fetal serum, etc. Submit information on manufacturer(s), quality certificates, controls performed. In the case of raw materials of animal origin, describe the origin and criteria for selection, shipping, and conservation, and submit a certificate on reduction of the risk of transmission of agents related to animal spongiform encephalopathy.

3.2. S.1.6 Analytical certificates signed by the manufacturer and the applicant for licensing.

3.2. S.2 MANUFACTURING PROCESS FOR ACTIVE INGREDIENT.



3.2. S.2.1 Manufacturer(s). Give the name, address, and responsibilities of the manufacturer(s).

3.2. S.2.2 Description of manufacturing process. Submit a description of the manufacturing process that includes all the stages. A typical production process for a vaccine starts with a vial(s) from the respective seed and / or cell bank, including cell cultures, harvest(s),

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

purification, modification reactions (when applicable), filling, storage, and transfer conditions. Where applicable, include the number of passes.

- Flow chart of manufacturing process. Showing all the manufacturing steps, including intermediate processes.
- Description of batch identification system. Identification of the lot in each stage of the process, including when mixtures are made. Also submit information on the manufacturing scale and lot size.
- Description of inactivation or detoxification process. Methods and agents used, parameters controlled, and production stage in which it is performed, when applicable.
- Description of purification process. Method, reagents, and materials used, operating parameters controlled, and specifications. Conditions for the use and re-use of membranes and chromatography columns and the respective validation studies.
- Description of conjugation process. Indicate when applicable and/or when a modification of active ingredient is done. Also include information on the origin and quality control of the starting material used to obtain the substance used as protein carrier.
- Stabilization of active ingredient. Description of the steps performed to stabilize the active ingredient, for example, the addition of stabilizers or other procedures, when applicable.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Reprocessing. Description of the procedures established for reprocessing the active ingredient or any intermediate product; criteria and justification.
- Filling procedure for the active ingredient, in-process controls. Description of the procedure for packaging the active ingredient, process controls, acceptance criteria, type of container closure system, type of seal on the container used to store the active ingredient, storage and transfer conditions, when applicable.

3.2. S.2.3 M a t e r i a l controls

3.2. S.2.4 Identification of critical steps in-process and controls.

Selection and justification of critical steps, starting from inoculation up to the production of the active ingredient, defining the operational parameters to control during the critical stages, including quality specifications should be included.



3.2. S.2.5 Validation of manufacturing process.

Description of changes.

Information on validation procedures and/or evaluation of the manufacturing procedures, including reprocessing, establishment of critical steps, and criteria for establishing the control limits on the critical steps.

3.2. S.3 CHARACTERIZATION OF ACTIVE BIOLOGICAL SUBSTANCE.

Present data to determine the structure and physicochemical, immunological, and biological characteristics of the active ingredient.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

3.2. S.4 *QUALITY CONTROL OF ACTIVE BIOLOGICAL SUBSTANCE*

3.2. S.4.1 Specifications

3.2. S.4.2 Analytical procedures

3.2. S.4.3 Validation of analytical procedures

3.2. S.4.4 Batch analysis and consistency results

3.2. S.4.5 Justification of specifications

3.2. S.5 REFERENCE STANDARDS OR MATERIALS.

Detailed description of the reference standards or materials used and analysis certificates.

3.2.S.6 PACKAGING/CONTAINER CLOSURE SYSTEM.



Full description of the packaging and container closure system in which the active ingredient will be stored until used for preparing the finished product. The information should include identification of all the materials that constitute the packaging container closure system and their specifications. When applicable, discuss the types of materials selected with respect to protection of the active ingredient against humidity and light.

3.2. S.7 STABILITY OF ACTIVE INGREDIENT

3.2. S.7.1 PROTOCOL OF STABILITY STUDY, SUMMARY AND CONCLUSIONS.

Should include the study conditions, including all the storage conditions (temperature, humidity, light) in which the vaccine is evaluated, analytical method, specifications, summary of results, and conclusions.

3.2. S.7.2 POST-APPROVAL STABILITY PROGRAM.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

It refers to the continuation of the stability study, including the number of lots to be included in the study each year and the tests to be performed.

3.2. S.7.3 STABILITY DATA.

Should include complete data from each batch evaluated during stability studies.

3.2. S.7.4 S T O R A G E AND SHIPPING CONDITIONS OF ACTIVE INGREDIENT.

When applicable, describe the equipment used, areas, and buildings (if pertinent) and the shipping and storage conditions.

3.2. S.8 CONSISTENCY OF PRODUCTION OF ACTIVE INGREDIENT.

Summary protocol of the production and control of three consecutive lots of active ingredient, analysis certificates in the event this information is not included in the summary protocol for the finished product, an analysis of the results of these lots in terms of production consistency.

3.2. P FINISHED PRODUCT

3.2. P.1 DESCRIPTION AND COMPOSITION OF FINISHED PRODUCT.

This should include a description of the finished product, its composition, listing each of the components, active ingredient(s), adjuvant, preservatives, stabilizers, and excipients, stating the function of each of them. For lyophilized products, also include a description of the diluents and the container closure system employed for the diluents.

3.2. P.2 PHARMACEUTICAL DEVELOPMENT.



**Title: GUIDELINES FOR
THE REGISTRATION OF
VACCINES**



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

Information on the studies performed to establish the dosage form, formulation, manufacturing process, and the container closure system used for final product. The studies described in this point are different from the routine quality control tests performed in accordance with the product specifications. Include the following aspects:

3.2. P.2.1 ACTIVE INGREDIENT

Compatibility employed in the manufacturing process. It is also necessary to provide information on the viral safety of the product, when applicable.

3.2. P.3.6 DESCRIPTION OF BATCH IDENTIFICATION SYSTEM.

Define the lot in the stages of filling, lyophilization (if it applies) and packaging.

**3.2.P.4 CONTROL OF ADJUVANT, PRESERVATIVE, STABILIZERS AND
EXCIPIENTS**

3.2. P.4.1 SPECIFICATIONS

Provide information on the specifications for all the substances employed in the formulation of the finished product that are different from the active ingredient.

3.2. P.4.2 ANALYTICAL PROCEDURES.

Description or literature of reference of the methods used to control these substances.

3.2. P.4.3 VALIDATION OF ANALYTICAL PROCEDURES.

Include used procedures to control substances employed in formulating the final product.

3.2. P.4.4 JUSTIFICATION OF SPECIFICATIONS.

Include the information of all substances used in formulating the final product.

3.2. P.4.5 SUBSTANCES OF HUMAN OR ANIMAL ORIGIN.



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

Provide information on the source, origin, description of the quality tests performed, specifications, determination of adventitious agents, and viral safety.

3.2.P.4.6 USE OF NEW ADJUVANT, PRESERVATIVES, STABILIZERS AND EXCIPIENTS.

When used for the first time in a vaccine for human use or for a new route of administration, provide all information on the manufacture, characterization, and control, and data supporting safety established in nonclinical and clinical studies in relation to the active ingredient used.

3.2. P.5 CONTROL OF FINISHED PRODUCT

3.2. P.5.1 SPECIFICATIONS.

Indicate the specifications for the finished product.

3.2. P.5.2 ANALYTICAL PROCEDURES.



Information on the analytical procedures used for quality control of the finished product. For non-Pharmacopeia methods summaries or references are not accepted. Additional information could be requested.

3.2. P.5.3 VALIDATION OF ANALYTICAL PROCEDURES.

Include information on the validation of the analytical procedures for the finished product including experimental data.

3.2. P.5.4 BATCH ANALYSIS AND CONSISTENCY RESULTS.

The production and control protocols for at least three lots of finished product should be submitted and an analysis of the results for those lots in terms of production consistency.

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

3.2. P.5.5 DETERMINATION AND CHARACTERIZATION OF IMPURITIES.

As applicable, depending on the method used to manufacture the vaccine submitted for licensing.

3.2. P.5.6 JUSTIFICATION OF SPECIFICATIONS.

Provide justification of the specifications proposed for the finished product.

3.2.P.5.7 Analytical certificates signed by manufacturer and applicant for licensing

3.2.P.6 REFERENCE STANDARDS OR MATERIALS.

Provide information on the reference standards and/or materials used in the tests to control the finished product.

3.2.P.7 PACKAGING/CONTAINER CLOSURE SYSTEM

Describe in detail the type and form of container closure system of the finished product, including the materials of which they are made and quality specifications.

3.2. P.8 STABILITY

3.2. P.8.1 PROTOCOL OF STABILITY STUDY, SUMMARY AND CONCLUSIONS.

Submit the stability study that complies with each Sierra Leone's legislation, including the study protocol, specifications, analytical methods, detailed description of the container closure system for the product evaluated, storage conditions (temperature and relative humidity), summary of results for at least three lots of finished product prepared from different lots of active ingredient, conclusions, and proposed validity period. The stability studies should be signed by the professional in charge of the study. It is important to provide additional studies on the stability of the vaccine in



**Title: GUIDELINES FOR
THE REGISTRATION OF
VACCINES**



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

intermediate stages in the manufacturing method that require different temperatures from the storage temperature, studies of challenge temperatures, photosensitivity or other specifications, depending on the type of vaccine, evaluated for at least three lots. For lyophilized vaccines demonstrate the compatibility between the lyophilized product and the diluents.

3.2. P.8.2 POST-APPROVAL STABILITY PROGRAM.

Include the stability program or stability commitment to be carried out once the vaccine is in the market, including the number of lots to be included in the study each year and the tests to be performed. These results should be submitted periodically to update the information on the stability of the vaccine evaluated.

3.2. P.8.3 STABILITY DATA.

Should include the complete results of each lot evaluated during stability studies.

3.2. P.8.4 DESCRIPTION OF PROCEDURES TO GUARANTEE COLD CHAIN.

Describe in detail the measures used to guarantee adequate temperature and humidity conditions for shipping the finished product from the place of production to the place of final sale, including all the storage and distribution stages and indicating the controls performed in each of the stages. This description should be signed by the professional responsible for it.

3.2. A APPENDIX.

Provide the following information in the appendixes to Module 3:

3.2.A.1 EQUIPMENT AND FACILITIES.



	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

Diagram illustrating the production flow, including materials, personnel, waste, and intermediate products in relation to the manufacturing areas; information on adjacent areas related to protection and maintenance of the integrity of the vaccine. Also submit information on all the products prepared and/or handled in the same areas as the product submitted for licensing. Describe the procedures to avoid cross-contamination of areas and equipment.

3.2.A.2 SAFETY EVALUATION OF ADVENTITIOUS AGENTS.

Additional, detailed information on evaluation of the safety of the product in relation to adventitious agents of both viral and non-viral origin should be submitted.

3.3 LITERATURE REFERENCES

MODULE 4

NON CLINICAL INFORMATION

Non-clinical studies should comply with the WHO's Guidelines on Non-clinical Evaluation of Vaccines, WHO Technical Report Series No. 927, 2005, or most recent version.

4.1 TABLE OF CONTENTS OF MODULE 4



4.2 REPORT ON STUDIES

4.2.1 PHARMACOLOGY

4.2.1.1 Pharmacodynamic studies (immunogenicity of the vaccine)

4.2.1.2 Pharmacodynamic studies of adjuvant (if applicable)

4.2.2 PHARMACOKINETICS

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

4.2.2.1 Pharmacokinetics studies. When applicable, depending on the type of vaccine or when new substances are used in the formulation of the product, new routes of administration, or pharmaceutical forms that require the respective pharmacokinetic evaluation.

4.2.3 TOXICOLOGY



4.2.3.1 General toxicology. Information should be presented on:

- Design of study and justification of animal model
- Animal species used, age and size of groups
- Dose, route of administration and size group
- Parameters monitored
- Local tolerance

4.2.3.2 Special toxicology (for vaccines to which it applies). Information should be presented on:

- Special immunological investigations
- Toxicity studies in special populations
- Genotoxicity and carcinogenicity studies, when applicable
- Reproductive toxicity studies for vaccines to be administered to pregnant women or individuals of fertile age.

4.2.3.3 Toxicity of new substances used in formulation (new adjuvant, stabilizers, and additives).

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

In the case of new substances incorporated into the formulation (new adjuvants, stabilizers, additives) other routes of administration, and new combined vaccines, submit the corresponding toxicology studies.

4.2.4 SPECIAL CONSIDERATIONS

4.2.4.1 For attenuated vaccines evaluation of possibility of microorganism shedding through natural avenues of excretion should be submitted.

4.3 LITERATURE REFERENCES

MODULE 5

CLINICAL INFORMATION

The clinical studies should follow the WHO's Guidelines on Clinical Evaluation of Vaccines: Regulatory Expectations. WHO Technical Report Series No. 924, 2005, or most recent version, and the PBSL's guidelines for Clinical Trials.

GENERAL COMMENTS

Before beginning the clinical studies, it is necessary to have in-depth knowledge of the epidemiology of the pathogens or disease of interest in the study population. This knowledge makes it possible to statistically define the size of the sample required for the studies and to weigh the magnitude of the results for efficacy and safety.

All clinical studies should comply with the international and local standards for good clinical practices.



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

The clinical studies necessary to evaluate the clinical efficacy of a vaccine that contains one or more new antigens can involve substantial requirements with regard to the size of the population, compared to known and previously evaluated antigens. It is reasonable to require immunogenicity and safety studies only for vaccines that contain known, widely-used antigens and where safety/reactogenicity/immunogenicity of protection have been well established.

5.1 TABLE OF CONTENTS OF MODULE 5

5.2 CONTENTS: REPORTS OF CLINICAL STUDIES

PHASE I STUDIES

These are intended to define the safety and reactogenicity of the vaccine and to seek preliminary information on immunogenicity. Dose and route of administration should be evaluated with respect to these parameters. Generally these studies are conducted on small groups of immune competent healthy adults (50 to 200) who present low risk of being infected by the vaccine or related complications.

PHASE II STUDIES

After the studies in phase I have been completed or sufficient information is obtained to demonstrate satisfactory results, the phase II studies can begin. The main distinction between the two phases is that the phase II studies involve a large number (200 to 600) of subjects and are usually controlled and randomized. The main objectives of these studies are to demonstrate the immunogenicity of the active



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

component(s) and safety in the target population (mainly healthy children). The phase II studies should define the optimum dose, the vaccination schedule, and most importantly, safety, prior to beginning phase III.

PHASE III STUDIES

The Phase III studies are large scale studies designed to obtain data on the efficacy and safety of the vaccine. These studies are usually carried out in large populations to evaluate the efficacy and safety to the formulation(s) of the immunologically active component(s). Several thousand subjects can be enrolled in these studies (the number will be defined by the end point of the study). Serological data are collected (for at least one immunized population subgroup) with the idea of establishing a correlation between clinical efficacy and immunogenicity, although this cannot always be established.

- The type of vaccine and other relevant factors (incidence of disease, immunological markers, and safety) will determine the duration of the follow-up on these studies and the number of participants.
- The phase III clinical studies should be performed using at least three lots manufactured on the industrial or production scale to be used routinely (in the majority of countries).

SPECIAL CONSIDERATIONS

Depending on the type of vaccine, apart from the clinical studies on immunogenicity, efficacy, and reactogenicity, it may be necessary to evaluate microorganism shedding



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

in the case of live vaccines, interaction with other vaccines, and interference with maternal antibodies.

ADJUVANT

Evidence and scientific support that justifies the use of adjuvant, when applicable.

COMBINED VACCINES OR VACCINES MADE BY NEW MANUFACTURERS

Submit information on bridging studies performed to ensure the non-inferiority of the vaccine under evaluation compared with the reference vaccine, supporting immunogenicity, reactogenicity, safety, and efficacy, when applicable.

CO-ADMINISTRATION STUDIES WITH OTHER VACCINES



5.3 CLINICAL STUDY REPORTS

5.3.6 PHASE IV STUDIES AND/OR PHARMACOVIGILANCE PLAN (IF APPLICABLE).

Depending on the type of application for registration approval in other countries, or depending on the type of vaccine, a phase IV study protocol or the results of studies that have already been performed will be required. For new vaccines, a pharmacovigilance and a risk management plan depending on the type of vaccine should be presented.

5.4 LITERATURE REFERENCES

All literature references used in the study.



	<p>Title: GUIDELINES FOR THE REGISTRATION OF VACCINES</p>	
<p>Rev No: 02</p>	<p>Doc No: PBSL/GL/032</p>	<p>Version no. 03</p>
<p>Issue date: 15 May 2024</p>	<p>Effective date: 17 May 2024</p>	<p>Approved by: Registrar</p>

6.0 REFERENCES

1. Guide to Care and Use of Experimental Animals, CCAC, 1993. (Website: <http://www.ccac.ca>)
2. Target Animal Safety Guidelines for New Animal Drugs. Office of New Animal Drug Evaluation. Centre for Veterinary Medicine, Food and Drug Administration, Rockville , MD 20855 , USA . 2001.
3. Uses of Antimicrobials in Food Producing Animals. Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, 2002. (http://www.hc-sc.gc.ca/dhp-mps/pubs/vet/amr-ram_final_report-rapport_06-27_cp-pc-eng.php)
4. http://www.hc-sc.gc.ca/dhp-mps/vet/legislation/guide-ld/vdd_nds_guide-eng.php#7
5. <https://www.fdaghana.gov.gh/branches.php>
6. www.who.int/news/item

7.0 APPENDICES

APPENDIX I

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

RISK MANAGEMENT PLAN (RMP)

A Risk Management Plan (RMP) is a set of pharmacovigilance activities and interventions designed to identify, characterize, and manage risk relating to a medicine. The plan encompasses the entire life cycle of the product, and has to be periodically updated to reflect new knowledge and understanding of the safety profile of the product. Thus, the applicant is responsible for:



- developing a RMP
- updating the RMP as new safety information emerges
- implementing the activities and interventions outlined in the RMP
- Collecting information and performing an analysis regarding the efficacy of these activities and interventions
- Communicating this information to the PBSL in a timely manner.

The PBSL will request that a RMP is submitted before the biological product is registered. Also, the GHPBSL can request a RMP be submitted for a biological product which has already been registered, when a safety issue arises.

A RMP should include, but not limited to the following:

- an overview of the safety profile of the biological product
- a pharmacovigilance plan
- a risk management plan

A RMP should be submitted:



	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

❖ with an application for;

- any biological medicinal product containing a new biological drug substance
- a highly similar biological medicinal product
- a hybrid medicinal product where the reference product has a RMP and a safety concern requiring additional risk minimization activities has been identified with the reference biological medicinal product
- with an application for paediatric use registration application
- with an application involving a significant change in registration approval (e.g. new dosage form, new route of administration, new manufacturing process of a biotechnologically derived product, significant change in indication, including new paediatric indication) unless it has been agreed with the PBSL that submission of a RMP is not required
- on the request of the PBSL (pre- and post-registration)
- in the initiative of applicant/ marketing Authorization holder when they identify a safety concern with a biological medicinal product at any stage of the life cycle of the product

In some cases, biological medicinal products not listed in the above category may require a RMP, e.g.

- known biological drug substance
- hybrid biological medicinal products where the changes relative to the reference medicinal biological product suggest different risks

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar



- combination therapy application

Applicants should consult the PBSL on any questions they may have about their responsibilities relating to this section of the guidelines.

APPENDIX II

OUTLINE OF THE EVALUATION OF APPLICATION

- ❖ The authority in considering an application,
 - Shall satisfy itself that there is a need to have the product registered in Sierra Leone
 - Shall request the applicant to submit a manufacturer's authorization to register the product.
 - May consult with other bodies and experts with knowledge of the product.
 - Reserves the right to conduct a Good Manufacture Practice (GMP) audit inspection on the manufacturing facility for the product at a fee prescribed by the Authority.
 - An appeal for the review of an application may be made in writing to the Authority within 60 (Sixty) days of receipt of the rejection notice.
 - Where the Authority is satisfied that there is the need to register a product, and all requirements for its registration have been satisfied, it shall do so and issue to the applicant a certificate of registration, subject to such conditions as may be prescribed by the Authority from time to time.



	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- The registration of a product under these regulation, unless otherwise revoked, shall be valid for a period of 3 (three) years and may be renewed.
- The Authority shall from time to time, publish a notice in the Gazette notifying the registration of a product under these regulations.
- No information given in this application shall be disclosed by the Pharmacy Board of Sierra Leone to a third party, except;
 - With the written consent of the licence holder
 - In accordance with the directive of the Board of Directors of the PBSL
 - For the purpose of a legal process

APPENDIX III

SANCTIONS AND PENALTIES

- ❖ The Authority shall cancel, suspend or withdraw the registration of a product if:
 - The information on which the product was registered is later found to be false
 - The circumstances under which the product was registered no longer exist
 - Any of the provisions under which the product was registered has been contravened
 - The standard of quality, safety and efficacy as prescribed in the documentation for registration is not being complied with

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar



- The premises in which the product or part thereof is manufactured, packaged or stored by or on behalf of the holder of the certificate of registration is unsuitable for the manufacture, package or storage of the product.
- ❖ Where the registration of the product is suspended, withdrawn or cancelled, the Authority shall cause the withdrawal from circulation of that product and shall accordingly cause the suspension, cancellation or withdrawal to be published in the Gazette.

APPENDIX IV:



RELEVANT INFORMATION TO BE INCLUDED IN DOSSIER

In addition to the product registration requirements contained in the application form and this guidance document, please ensure that the information below is included in the dossier submitted for the registration of the biological products.



- Evidence of payment for evaluation and registration (a copy of payment receipt)
- Covering letter (Applicant)
- Covering letter (Local agent)
- Table of Contents
- Application form (Dated, stamped and signed)
- Signed Declaration
- Manufacturing License
- Contract Agreement Documents
- Contract Agreement Documents

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Application Overview (content: section 1)
- Full characterization of the host organism including the relevant genotypic and phenotypic properties
- Certificate of Analysis of Master Cell Bank/Master seed Lot (Protocol and report to qualify MCB/MSL)
- Certificate of Analysis of Working Cell Bank/Working Seed Lot (Protocol and report to qualify WCB/WSL)
- Certificate of Analysis of Starting Raw Materials (cDNA, vector, expression system), (from supplier)
- Certificate of Analysis of Starting Raw Materials (cDNA, vector, expression system), (from manufacturer)
- Certificate of Analysis of Inactive Raw materials (enzymes including; restriction enzymes, phosphatase, polymerase, transcriptase, S1, etc., buffer ingredients, growth media and additives, compressed gases, etc.)
- Complete Drug Master File (DMF) containing development genetics, protein expression
- Protocols, protein purification protocols, protein identification and characterization formulation, etc.
- Map of empty expression vector/ map of expression construct
- Genetic make-up of empty expression vector and expression system
- Report on genetic make-up of empty expression vector and expression system
- Report on genetic material coding desired biological drug substance (API)

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Relevant genotype and phenotype of host organism
- Report on the choice of host organism
- Report on process validation
- Evidence of purchase of reference product
- Protocol and report for isolation of reference product drug substance, (if applicable)
- Certificate of Analysis of biological drug substance
- Protocol and report of analytical method of validation (AMV) for drug substance reference product (if applicable)
- Protocol and Report of analytical method validation (AMV) for reference product (if applicable)
- Protocol and Report of analytical method validation (AMV) for drug substance of biological Medicinal product
- Protocol and Report of analytical method validation (AMV) for finished biological medicinal product
- Analytical Control Procedures
- BMR for finished biological medicinal product (Should be recent and in English language)
- Protocol and report of process validation
- Certificate of Pharmaceutical Product/Certificate of Analysis of biological drug product



	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

- Batch release abstract and Batch release document (completed, dated and signed)
- Protocol and report for real time/long term stability studies
- Protocol and report for accelerated stability studies
- Protocol and report for stress stability studies
- Protocol and report on non-clinical and clinical studies
- Protocol and report on animal studies (if applicable)
- Quantity and number of reference product received (client service, PBSL)
- Quantity and number of samples (biological medicinal product) received (client service, PBSL)
- Programme for post-market surveillance/Pharmacovigilance and risk management plan
- Report on substitution and interchangeability (if applicable)
- Package Insert

APPENDIX V:

RELEVANT PBSL GUIDANCE DOCUMENTS

- I. Guidelines for Registration of Biological products
- II. Guidelines for Safety Monitoring
- III. Guidelines for conducting clinical trials of allopathic drugs, VACCINES, and medical devices

	Title: GUIDELINES FOR THE REGISTRATION OF VACCINES	
Rev No: 02	Doc No: PBSL/GL/032	Version no. 03
Issue date: 15 May 2024	Effective date: 17 May 2024	Approved by: Registrar

IV. Guidelines for requirements for labelling of products.

APPENDIX VI:

APPENDIX VII:

Batch release document for vaccines, refer to www.pharmacyboard.gov.sl

APPENDIX VIII:

Application form for the registration of biological products including vaccines, refer to www.pharmacyboard.gov.sl

ABBREVIATIONS AND ACRONYMS

AMV	Analytical Method of Validation
API	Active Pharmaceutical Ingredient
BMR	Batch Manufacturing Record
cGMP	current Good Manufacturing Practice
EPC	End of Production Cells
PBSL	Pharmacy Board of Sierra Leone
MCB	Master Cell Bank
MSL	Master Seed Lot
RMP	Risk Management Plan
SRA	Stringent Regulatory Authority



Title: GUIDELINES FOR THE REGISTRATION OF VACCINES



Rev No: 02

Doc No: PBSL/GL/032

Version no. 03

**Issue date: 15 May
2024**

Effective date: 17 May 2024

Approved by: Registrar

WCB

Working Cell Bank

WHO

World Health Organization

WSL

Working Seed Lot

Prepared by

Reviewed by

Approved by

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Head, Quality Assurance

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