RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES FOR REGISTRATION OF IMMUNOLOGICAL VETERINARY PRODUCTS

AUGUST, 2025

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FOREWORD

Rwanda Food and Drugs Authority (Rwanda FDA) is a regulatory body established by the Law N° 003/2018 of 09/02/2018. One of the functions of Rwanda FDA is to regulate matters related to quality, safety, and efficacy of Immunological Veterinary Products to protect public health by increasing access and availability of essential medicines.

In consideration of the provisions of the technical regulations N° DFAR/HMDAR/TRG/001 Rev_3 of 28th September 2022 governing the registration of pharmaceutical products, which recommends issuing guidelines. Rwanda FDA has issued Guidelines *No: Doc. N°.: DD/VMDR/GDL/003 Version 2 for registration of Immunological Veterinary Products."*

These Guidelines have therefore been reviewed in order to cope with the new developments in line with the requirements for marketing authorisation. They provide guidance on the content and format of information to be presented in registration dossiers submitted to Rwanda FDA for registration of veterinary biological products in Rwanda.

Adherence to the guidelines by the manufacturers/applicants will facilitate timely assessments and approvals of biological product application dossiers for marketing authorization. Rwanda FDA acknowledges all the efforts of key stakeholders who participated in the development and validation of these guidelines.

Prof. Emile BIENVENU
Director General

Digitally signed by RWANDA FDA(Director General)
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DOCUMENT REVISION HISTORY

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21/12/2021	1	First Issue
22/07/2025	2	1. Adoption of the new Guidelines template according to the updated SOP on document control 2. Addition of some definitions 3. Change of mode of application submission 4. Update of the registration certificate content and format 5. Update on the title (Name) of the guideline 6. Update on submission requirements 7. Addition of cover letter in appendices 8. Update on timelines for product registration 9. Editorial changes

TABLE OF CONTENTS

DOCUMENT DEVELOPMENT HISTORY 3
TABLE OF CONTENTS 4
ACRONYMS AND ABBREVIATIONS 5
GLOSSARY / DEFINITIONS 6
CHAPTER ONE: INTRODUCTION 9
I.1 Background 9
I.2 Scope 9
I.3 Preparation And Presentation Of Information In Ctd Format 10
I.4 Submission Of Application 10
I.5 Types Of Product Registration Applications 11
I.5.1 New Registration Applications: 11
I.5.2 Renewal Of Product Registration: 11
I.5.3 Variation Of A Registered Product: 11
I.5.4 Annual Retention 11
CHAPTER II: ORGANIZATION OF THE COMMON TECHNICAL DOCUMENT (CTD) 15
MODULE 1: ADMINISTRATIVE INFORMATION 15
MODULE 2: OVERVIEWS AND SUMMARIES 18
MODULE 3: QUALITY INFORMATION 19
3.2.S Immunogenic Substance(S) 19
3.2. S.1. General Information 19
3.2. S.2. Manufacturing Process For The Immunogenic Substance(S) 20
3.2. S.3. Manufacturing Consistency 22
3.2. S.4. Reference Standards Or Materials 22
3.2. S.5. Container And Closure System 22
3.2. S.6. Stability Of Immunogenic Substance 23
3.2.P Immunological Veterinary Product (Ivp) 23
3.2. P.1 Description And Composition Of The Ivp 23
3.2. P.2 Method Of Manufacture 24
3.2.P.3 Control Tests On The Finished Product 26
3.2.P.4 Batch To Batch Consistency 27
3.2.P.5 Containers 28
3.2.P.6 Stability Of The Final Immunological Veterinary Product 28
MODULE 4: SAFETY 31
MODULE 5: EFFICACY 34
ENDORSEMENT OF THE GUIDELINES 35

ACRONYMS AND ABBREVIATIONS

EMA	European Medicines Agency,
EMEA	European Medicines Evaluation Agency
Ph. Eur	European Pharmacopoeia
CTD	Common Technical Document
Hrs	Hours
GMP	Good Manufacturing Practice
MCS	Master Cell Seed
Rwanda FDA	Rwanda Food and Drugs Authority
rDNA	ribosomal DNA (Deoxyribonucleic acid)
TSE	Transmissible Spongiform Encephalopathy
VICH	International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products
IVP	Immunological Veterinary Product
WCS	Working Cell Seed

GLOSSARY / DEFINITIONS

The definitions provided below apply to the terms used in these guidelines. They may have different meanings in other contexts and documents. For these guidelines the following definitions shall apply:

"Antibody" A spectrum of proteins of the immunoglobulin family that are produced, in the human (or animal) body, in response to an antigen (e.g., a virus or bacterium, or a foreign protein unknown to the body's immune system). Antibodies can combine with and neutralize the antigen, as well as to stimulate the immune system for defense reactions.

"Antigen" A substance that causes the immune system to produce antibodies against it.

"Applicant" Means a person who applies for registration of a medicinal product to Rwanda FDA, who must be the owner of the product. He may be a manufacturer or a person to whose order and specifications, the product is manufactured. After the product is registered, the applicant shall be the "Marketing Authorisation Holder.

"Authority" The Rwanda Food and Drugs or its acronym "Rwanda FDA", established under Article 2 of the Law N° 003/2018 of 09/02/2018.

"Batch" A total quantity of goods produced at one time.

"Distributor" A person or organization who receives, stores, warehouses, handles, holds, offers, markets or displays medical products. A distributor shall be an entity that is appropriately authorized by the competent authority to perform the function as prescribed in these regulations, and which can be held accountable for its activities. These include but are not limited to governments at all levels, public and private health and storage facilities, manufacturers of finished products, importers, exporters, distributors, wholesalers, suppliers, retailers.

"Excipient" Any pharmacologically inert substance used for combining with an active substance to achieve the desired bulk, consistency, etc.

"Finished Product" The formulated medicinal product containing the active ingredient(s) and ready for administration either alone or after reconstitution with the relevant diluents.

"Immunogenic Substance" Any substance that is recognized as foreign by the immune system in a (particular) higher organism and induces an immune response which may include the formation of antibodies and developing immunity, hypersensitivity to the antigen, and tolerance.

"Immunological Veterinary Product" A veterinary medicinal product with an immunological mode of action, i.e. it induces immunity to the active substance(s) contained in a product.

"Local Technical Representative" Means any registered company in Rwanda and licensed by Rwanda FDA to deal with regulated products that has received a mandate from the Applicant to act on his/her behalf with regard to matters pertaining to the registration of regulated products.

"Marketing Authorization /Registration certificate" Approval from the authority necessary to market and sell a product in Rwanda. This is a legal document that establishes the detailed composition and formulation of the product and the pharmacopoeia or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labelling and shelf-life. It is also a legal document issued by the Authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy and quality.

"Marketing Authorisation Holder (MAH)" A person granted with a marketing Authorization of a product by an NRA.

"Manufacturer" A company that carries out operations such as production, packaging, repackaging, labelling and relabelling of products regulated by Rwanda FDA.

"Master Cell Seed (MCS)" Collection of aliquots of preparation of cells, for use in the preparation of a product, distributed into containers in a single operation and processed together in such a manner as to ensure uniformity and stored in such a manner as to ensure stability.

"Master Seed (MS)" A collection of aliquots of preparation, for use in the preparation and testing of a product, distributed into containers in a single operation and processed together in such a manner as to ensure uniformity, and processed and stored in such a manner as to ensure stability.

"Primary Cell Cultures" Cultures of cells, essentially unchanged from those in the animal tissues from which they have been prepared, and being no more than 5 in vitro passages to production level from the initial preparation from the animal tissue.

"Seed Lot System" A system according to which successive batches of product are prepared using the same Master Cell Seed or Master Seed.

"Specifications" A list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which an Immunogenic substance, Immunological Veterinary Product, or materials at other stages of its manufacture should conform to be considered acceptable for its intended use. 'Conformance to specification' means that the Immunogenic substance and Immunological Veterinary Product, when tested according to the listed analytical procedures,

will meet the acceptance criteria. Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities as conditions of approval.

"Vaccine" A preparation of weakened (attenuated) or killed pathogens, such as a bacterium or virus, or of a portion of the pathogen's structure, that stimulates immune cells to recognize and attack it, especially through the production of antibodies.

"Validation" The process of demonstrating that the system (or process) under consideration meets in all respects the specification of that system or process. Also, the process of evaluating a system or component during or at the end of the development process to determine whether it satisfies specified requirements.

"Wholesaler" An entity that is authorised to carry on the business of selling medical products in large quantities to other authorised sellers with the exception of dispensing or providing medical products directly to a patient.

"Withdrawal period" The minimum time that must elapse between the cessation of treatment of a food-producing animal and either the slaughter of the animal for human consumption or the resumption of the supply for human consumption of products, such as eggs, milk derived from the animal.

"Working Cell Seed (WCS)" A collection of aliquots of preparation of cells, for use in the preparation and testing of a product, consisting of cells of a passage level intermediate between Master Cell Seed and those used for production, distributed into containers in a single operation and processed together in such a manner as to ensure uniformity, and processed and stored in such a manner as the ensure stability.

"Working Seed Lot" A collection of aliquots of a preparation consisting of a passage level between Master Seed and the last passage, which forms the finished product, for use in the preparation of finished product, distributed into containers in a single operation and processed together in such a manner as to ensure uniformity, and processed and stored in such a manner as to ensure stability.

CHAPTER ONE: INTRODUCTION

I.1 Background

These guidelines were developed to guide applicants who intend to register immunological products for veterinary use in Rwanda. They were developed based on the East African Community's guideline on the technical documentation required to be included in a registration dossier for an immunological veterinary product (IVP) and the Tanzania guidelines for registration of immunological veterinary products. Additionally, other relevant international guidelines and documents were consulted for guidance and consolidation of this document. The present guidelines have been prepared by taking into consideration the need for a regional and worldwide harmonization, which will assist in the preparation and assessment of a well-structured dossier to be submitted for the registration of immunological veterinary products on the Rwandan market.

This document provides details about the type of Quality information concerning the Manufacture and Control of an immunological veterinary product that the applicant should include in the registration application dossier. It also describes the data required to support the Safety and the Efficacy of the product. In addition, these guidelines describe administrative information to be included in the application dossier. The guidelines set out procedures and requirements for the application for registration of immunological veterinary products using the Common Technical Document (CTD). The CTD format has five Modules:

Module 1: Administrative Requirements;

Module 2: Overview and Summaries of veterinary immunogenic substance(s) and immunological veterinary product;

Module 3: Quality of the Veterinary immunogenic substance(s) and Immunological Veterinary Product;

Module 4: Safety of the Veterinary immunogenic substance(s) and/or Immunological Veterinary Product;

Module 5: Efficacy of veterinary immunogenic substance(s) and/or Immunological Veterinary Product.

I.2 Scope

These guidelines apply only to Immunological Veterinary Products intended for marketing in Rwanda. They describe data required to demonstrate that an Immunological Veterinary Product intended for marketing in Rwanda complies with the established requirements.

They should be read in conjunction with other international guidelines on quality, safety, and efficacy as cited in this guideline namely The World Organization for Animal Health (OIE), the European Medicines Agency (EMA), and Veterinary International Conference of Harmonization (VICH). Adherence to these guidelines by applicants will facilitate the timely review and processing of product registration.

I.3 Preparation and Presentation of Information in CTD format

The applicant shall prepare and present the product's information dossier in the CTD format according to the requirements as stipulated below:

(a) The application should be written in English, French or Kinyarwanda. Any document which is in any language other than English, French or Kinyarwanda must be accompanied by a certified or notarized translation;

(b) The application must contain a complete index of the various appendices;

(c) The Quality Overall Summary (QOS) should be formatted as a word document downloadable on Authority's website and the body data in Module 3 should be in PDF;

(d) All pages of the application should be numbered in the style: page x of y;

(e) The application should be submitted via Rwanda FDA Clients online portal Integrated Regulatory Information Management System (IRIMS CLIENTS);

(f) The PDF documents should be in Optical Character Recognition (OCR), selectable and searchable;

(g) A separate application is required for each product that differs in active ingredient(s), strength, dosage form, proprietary names though containing the same ingredients or is considered to be different products. However, products containing the same active ingredients and the same strength made by the same manufacturer at the same manufacturing site, to the same specifications and dosage form, but differing only in packing or pack sizes require only one application.

I.4 Submission of application

An application for registration of immunological veterinary products for either locally manufactured or imported shall be made in writing via a cover letter and application form dated and signed by the applicant.

The application shall be submitted through the Rwanda FDA online Portal (https://www.irims.rwandafda.gov.rw/portal/).

A reference number is automatically assigned to the application and it will be used in all subsequent correspondences relating to the application. An acknowledged receipt will be issued automatically by the system.

Two commercial samples of each pack size shall be submitted to the Rwanda FDA Head Office. Those samples should be accompanied by a cover letter **(Annex1)** and a printed notification email clearly stating the application reference number generated by the Rwanda FDA portal at the time of submission.

If the applicant is a foreign company, the applicant shall appoint a Local Technical representative (LTR) through whom an application shall be submitted. The appointment shall be notified to the Authority by submitting a letter of appointment supported by original copy of power of attorney duly notarized in country of origin, and a valid copy of the license issued by Rwanda FDA.

I.5 Types of Product Registration Applications

For submission of Product Dossier to Rwanda FDA, applications are classified into the following categories.

I.5.1 New registration applications

An application for registration of a product that is intended to be placed on the Rwandan market for the first time or a product which was on the market without a registration certificate.

I.5.2 Renewal of product registration

Applications for renewal of a registered product. The application shall be made at least 3 months before the expiry of existing registration according to requirements stipulated in the Rwanda FDA application guideline for renewal of the market authorization.

I.5.3 Variation of a registered product

An application for any change in the registered products. All applications for variation to a registered product shall be made according to requirements stipulated in the Rwanda FDA application Guideline for Variation of Registered veterinary products.

I.5.4 Annual retention

Application for retention of registered immunological veterinary products on the register should be submitted. Applications are submitted at least 2 months before the end of each year, from the date of issuing the market authorization (MA).

Application requirements for a registered immunological veterinary product retention include:

(a) Cover letter;
(b) Proof of payment of prescribed fees (Refer to regulations No: ODDG/RES/TRG/001 Rev_5 Governing Tariff/Fees and Charges on Services Rendered by Rwanda Food and Drugs Authority).

I.6 Application requirements

An application dossier for registration of IVPs in Rwanda shall include the following:

(a) Dated and signed cover letter (**Annex 1**);
(b) Dated and signed application form for product registration (**Annex 2**);
(c) Payment of registration fee in accordance with regulations governing tariff/fees and charges on services rendered by Rwanda Food and Drug Authority;
(d) CTD document Format in (PDF) and QOS in MS-Word;
(e) Two commercial samples of each pack size (The submission of samples should comply with the storage conditions as prescribed by the manufacturer to avoid any alteration of the product during transportation);
(f) Evidence of payment for the Rwanda FDA GMP inspection and proof of GMP inspection application for the IVP manufacturing site, or a GMP certificate issued by the Rwanda FDA.

I.7 Officially Recognized References

The official pharmacopoeias recognized by the Authority are: British Pharmacopoeia (BP), European Pharmacopoeia (Ph. Eur.), the International Pharmacopoeia (Ph.Int), Japanese Pharmacopoeia (JP) and United States Pharmacopoeia (USP). References should be cited following the current edition of compendia.

I.8 Harmonization with other international regulators

Rwanda FDA harmonizes its registration processes as much as possible with other competent, Stringent Regulatory Authorities (SRAs) and international organizations such as The World Organization for Animal Health (WOAH) and the Veterinary International Conference on Harmonization (VICH). Where specific guidelines are unavailable, Rwanda FDA adopts Committee for Medicinal Products Veterinary Use (CMPV) Guidelines, which are available at the following websites EMA: http://www.ema.europa.eu and Veterinary International Conference on Harmonization (VICH) Guidelines: https://www.vichsec.org/en/.

I.9 Rwanda FDA Dossier Assessment Procedures

I.9.1 Dossier assessment for product quality, safety and efficacy

After Rwanda FDA receives a complete product application dossier via IRIMS, the application will be scheduled for assessment according to the First In First Out (FIFO) rules. Priority assessment may be granted where the product is intended for the control of rare disease conditions or in the case of an emergency situation. For more detailed information, refer to the guideline for conditional approval of Veterinary Products.

Furthermore, an abridged assessment may be conducted in case a product is eligible for the reliance procedure using the guidelines on reliance for regulatory decision making and the guidelines for abbreviated assessment procedures for registration of veterinary products.

A product dossier is assessed by two assessors to provide scientific and regulatory oversight regarding the quality, safety, and efficacy of the product under assessment. Rwanda FDA reserves the right to request any additional information to establish the quality, safety, and efficacy of an immunological veterinary product.

During the assessment, additional data and/or samples may be requested through the system. Further processing of the application may only be undertaken if responses to queries issued contain all outstanding information requested in one submission. Failure to comply with this condition or if the queries have been reissued for the third time and the applicant provides unsatisfactory responses, the application will be rejected.

If the responses to the queries are not submitted within ninety (90) working days from the date they were issued, it will be considered that the applicant has withdrawn the application unless the applicant has requested for extension of the deadline to Rwanda FDA. Thereafter, registration of the product may only be considered upon submission of a new application.

I.9.2 Rwanda FDA Internal Scientific Review Committee for Product Registration

After the completion of the product dossier assessment, a final assessment report shall be presented to the Internal Scientific Review Committee for review and recommendation for Marketing Authorization approval or rejection.

In the event, that there are safety, quality, or efficacy issues to be resolved as per the decision of the Internal Scientific Review Committee, the application shall remain pending until the resolution of the raised issues.

Rwanda FDA will register the product which data on safety, quality, and efficacy are considered satisfactory and a registration certificate of Immunological veterinary products **(Annex 7)** will be granted. The registration shall be valid for five (5) years with annual retention. If Rwanda FDA suspends or cancels the registration validity, a written official communication shall be made to the applicant.

I.9.3 Compliance with the Good Manufacturing Practices (GMP)

The GMP inspection is part of the product registration process. Rwanda FDA should inspect the facility or use other means to verify whether the manufacturing site complies with GMP regulations and guidelines before a product is registered. No product shall be registered unless the facility complies with GMP. More information on GMP requirements and application for GMP inspection is detailed in the Rwanda FDA Guidelines on Good Manufacturing Practices and its annexes downloadable from Rwanda FDA website.

I.10 Timeline for product registration

Product dossiers shall be scheduled for assessment according to the First in First out (FIFO) basis upon compliance with the requirements. A new application shall be processed within twelve (12) months of receipt of the application (Figure 1).

The applicant will be required to provide any requested additional data within ninety (90) working days. Additional data or query responses shall be processed within sixty (60) working days. Once a query has been issued to the applicant, the assessment process clock stops until Rwanda FDA receives a written response to the raised queries.

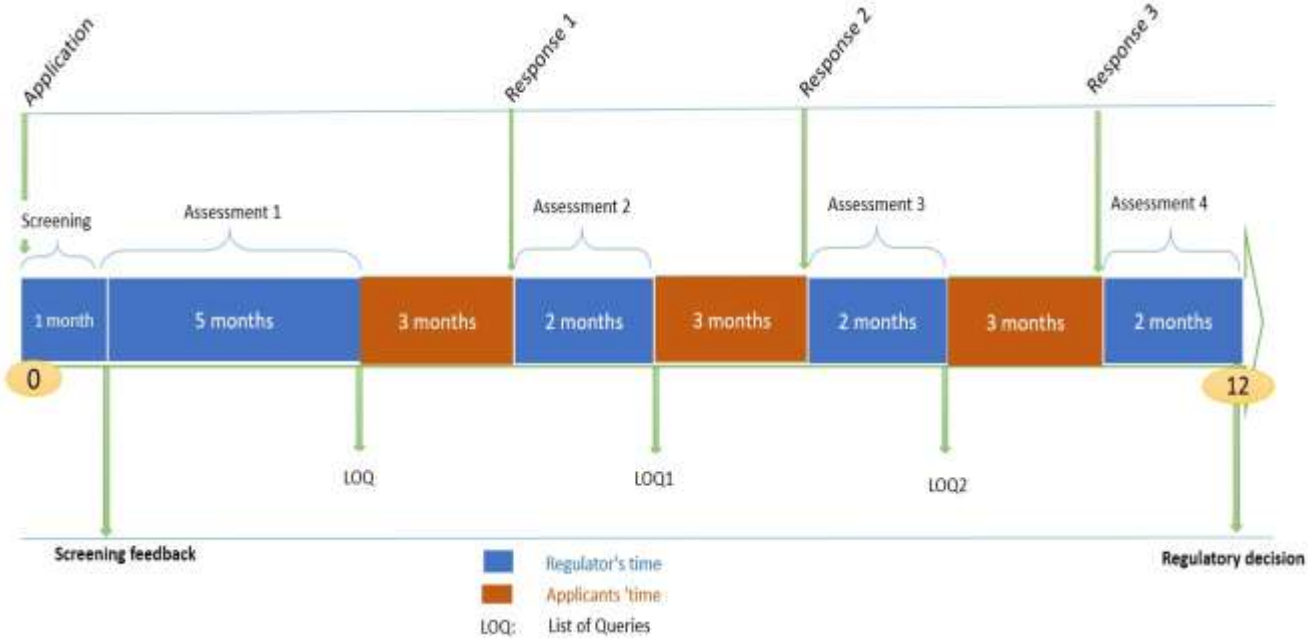

Figure 1. Graphical illustration of timelines

CHAPTER II: ORGANIZATION OF THE COMMON TECHNICAL DOCUMENT (CTD)

MODULE 1: ADMINISTRATIVE INFORMATION

Module 1 should contain all administrative documents such as the duly completed application form, certifications, letters, licenses, reports, annexes among others, as needed. Documents submitted in module one can be submitted as separate files or in one file. All applications and supporting documents should be either in English, French or Kinyarwanda. Any document which is in any language other than English, French or Kinyarwanda must be accompanied by a certified or notarized translation.

Documents should be organized in the order listed below: Generally, all of the documents in Module 1, other than the annexes, can be provided in a single volume. The annexes to the module should be submitted in separate volumes.

1.1. Comprehensive Table of Contents for all Modules

The table of contents should indicate the sections, subsections, and corresponding page numbers for the entire application.

1.2. Cover Letter

A dated and signed Cover letter should be submitted in the IRIMS with the product dossier clearly indicating the product name seeking a marketing authorization and the contact details of applicant (Name and detailed address).

1.3. Application form

An application for registration of immunological veterinary products on the Rwandan market must be accompanied by a duly completed application form. The application form should be duly filled with relevant information and attachments, dated, signed and stamped appropriately. If the applicant is not the manufacturer of the product, a duly signed and dated manufacturing agreement between the applicant and the actual manufacturer must be submitted. This agreement should clearly outline the roles and responsibilities of each party.

1.4. Manufacturing and Marketing Authorization

A valid manufacturing license/authorization or a valid Certificate of Pharmaceutical Product (CoPP), or an equivalent certificate issued by a competent authority of the country of origin to the manufacturer of the finished immunological product should be submitted. If applicable, a valid manufacturing authorization for the production of the diluent should also be provided. In addition,

valid manufacturing authorization(s) for the active immunogenic substance(s) manufacturer (s) should be provided.

1.5. Mock-Ups

Mock-ups of the sample(s) presentation of the immunological veterinary product available at the time of initial application should be submitted. The purpose of this, is to provide an example of the product including accessories, if any, to verify that they correspond to what is described for the characteristics of the product under evaluation.

1.6. Summary of Product Characteristics (SmPCs)

All applications for registration of immunological veterinary products should be accompanied by a summary of product characteristics (SmPCs). The SmPCs should be prepared following the content and the format as provided in **Annex 4.** After the assessment and the approval of the submitted SmPC, it will be published online. The consent from the applicant can be requested if applicable.

1.7. Container Labelling

Containers should be labelled as recommended in **Annex 5** of these guidelines. This should be provided as mock-ups.

1.8. Product Information Leaflet (PIL)

Every container of Immunological Veterinary Products should be accompanied by an information leaflet. One copy of the information leaflet prepared based on the provisions of **Annex 6** should be provided.

1.9. Product Samples

Two commercial samples of the finished product along with their certificates of analysis, labels, and cartons of the primary and secondary packaging of the product, including the package insert and accessories should be provided.
The number of samples can increase depending on the nature and type of the product applied for registration, ideally, samples should be provided to allow full monograph analysis.
The submission of samples should comply with the storage conditions as prescribed by the manufacturer to avoid any alteration of the product during transportation.

1.10. List of Countries where the Product has been Licensed and Summary of Approval Conditions

If applicable, the applicant should provide the list of countries where the product is registered at the time of the application for registration. In the event the product has been registered in other countries, copies of registration certificates should be attached.

1.11. Good Manufacturing Practice

A valid certificate of GMP compliance should be provided. This should include manufacturers that are involved in any stage of the production process, for example, the manufacturer(s) of the finished immunological product, Immunogenic substance(s), the diluents, and those responsible for labelling and packaging of the finished immunological product.
In addition, a copy of a GMP certificate issued by Rwanda FDA or proof of application and proof of payment to GMP inspection of the finished immunological product manufacturing site by Rwanda FDA should be submitted.

1.12. Authorization of the Local Technical Representative

Any applicant who is not resident in Rwanda shall appoint a local technical representative (LTR) who must be a registered company in Rwanda and licensed by Rwanda FDA to deal with regulated products that has received a mandate from the Applicant to act on his/her behalf with regard to matters pertaining to the registration of regulated products.

The appointment shall be notified to the Authority by submitting a letter of appointment supported by original copy of power of attorney duly notarized in country of origin, and a valid copy of the license issued by Rwanda FDA.

1.13. Certificates of Suitability of monographs of the European Pharmacopoeia (CEP) or APIMF

If CEP is available, applicants should present a copy of CEP and a Letter of Access to CEP as appropriate. Where reference is made to an Active Pharmaceutical Master File (APIMF), the applicant should provide the APIMF and a Letter of Access to the APIMF as appropriate.

MODULE 2: OVERVIEWS AND SUMMARIES

The purpose of this module is to summarize the quality, safety, and efficacy information presented in modules 3, 4, and 5 in the market authorization application. The information in module 2 should be presented in world format in the following order:

2.1. Table of contents

A table of content of module 2 should be provided.

2.2. CTD Introduction

A summary of the type of immunological veterinary product, composition, immunological mechanism, and proposed indications for the product should be provided.

2.3. Quality Overall Summary (QOS)

The Quality Overall Summary is a summary that follows the scope and the outline of the Body of Data in Module 3. The QOS should not include information, data, or justification that was not already included in Module 3 or other parts of the CTD. The QOS template is in **Annex 3** of this guideline. The QOS should be provided in a word version.

2.4. Summary of safety data

All the data related to safety assessed through the development of the product, as well as any study limitations, should be summarized and presented in this section. Summaries should include all the laboratory and field studies performed and a synopsis of each study.

2.5. Summary of efficacy data

All the data related to efficacy assessed through the development of the product, as well as any study limitations, should be summarized and presented in this section. Summaries should include all the laboratory and field studies performed and a synopsis of each study.

MODULE 3: QUALITY INFORMATION

3.1. Table of Contents of Quality Part

A table of content of the filed product dossier should be provided.

3.2. Body data

3.2.S Immunogenic substance(s)

The information requested under this section should be supplied individually for each immunological substance in the product and should be completed for each immunogenic substance identified as being present in the final immunogenic product.

3.2. S.1. General information

3.2.S.1.1 Nomenclature

Applicant provides a clear description of the immunogenic substance. The biological name (including strain and/ or clone designation) or chemical name, including any approved name, should be provided. The name(s) or designation of the strain of organism used to produce the active immunogenic substance should be provided.
The description should also include the source of the cells, including microbes from which the immunogenic substance was derived, the active components of the cell fractions or purified antigens, and the physical and chemical properties of the synthetic immunogenic substance.
Any chemical modification or conjugation of the immunogenic substance should be described in detail. Also, a list of any inactive substance, which may be present in the immunogenic substance, should be provided.

3.2.S.1.2 Structure

The structural formula and molecular weight should be provided. The schematic amino acid sequence indicating glycosylation sites or other post-translational modifications and relative molecular mass should be provided, as appropriate.

3.2.S.1.3 General Properties

A list of physicochemical and other relevant properties of the immunogenic substance, including biological activity, should be provided. The description of a rDNA- derived biotherapeutics should indicate the biological system in which it is reduced (e.g. bacterial, fungal, or mammalian cells) as well as the presentation of the finished product.

3.2. S.2. Manufacturing Process for the Immunogenic Substance(s)

3.2.S.2.1 Manufacturer(s)

The name(s) and physical address (es) of the manufacturer(s) of the immunogenic substance including activities performed at each manufacturing site should be provided. The facilities involved in the manufacturing, packaging, labelling, testing and storage of the active substance should be listed. The list of manufacturers/companies should specify the actual addresses of production or manufacturing site(s) involved (including block(s) and units(s). Telephone number(s), fax number(s), and e-mail address (es) should also be provided.

A valid certificate of GMP compliance should be provided for the active immunogenic substance. If available, a manufacturing authorization should be provided in Module 1.

3.2.S.2.2 Method of Manufacture

3.2.S.2.2.1 Flow chart of the manufacturing process

A complete visual representation of the manufacturing process flow should be provided for each active immunogenic substance. Steps in production, including incubation times and temperatures, equipment and materials used, the area where the operation is performed, and a list of the in-process controls and finished product tests performed at each step should be clearly shown. In-process holding steps should be included with time and temperature limits indicated.

3.2.S.2.2.2 Description of Manufacturing Process

A detailed description of each process step as presented in the flow chart substance should be provided.

A description of manufacturing starting with the Master Seed and procedures used to derive a Working Seed from the Master Seed should be provided. Media and the identification system used for the working Seed Bulk (WSB), as well as the procedures for storage and cataloging of the WSB and any steps in which the bulk of the active immunogenic substance is further processed (e.g separated from the cells, concentrated), should be provided. A list of all the components used in the manufacturing process including media, solvents, or solutions should also be provided.

A description should be provided for:

(a) Propagation and Harvest

For each Immunological substance/ antigen production method or combination of methods, a growth curve or tabular representation of growth characteristics for each propagation step should be provided. A table showing the yield, purity, and viability (if applicable) of the crude harvest should also be included.

(b) Inactivation (if appropriate)

Inactivation kinetics or killing curves, or a tabular representation should be provided. Validation of the titration method used to measure residual live organisms, including the sensitivity of the method in a background of inactivating agents, should be provided.

The following information should be provided:

(i) How Culture purity is verified before inactivation;
(ii) The method(s) and agent(s) used for inactivation;
(iii) The method(s) undertaken to prevent aggregation and assure homogeneous access of inactivating agent(s) to the culture;
(iv) The stage in production where inactivation or killing is performed;
(v) The parameters which are monitored.

(c) Detoxification (if appropriate)

For toxoid or toxoid-containing vaccines, the detoxification procedures should be described in detail for the toxin component(s):

(i) The method(s) and agent(s) used for detoxification;
(ii) The stage in production where detoxification is performed and the parameters, which are monitored, must be described.

(d) Purification (if appropriate)

Describe any purification methods used, including specialized equipment such as columns, ultracentrifugation, ultra-filtration, and custom reagents such as monoclonal antibodies. The process parameters monitored and the process for determination of yields should be stated. For each purification method or combination of methods used, a tabulation of yields, purity and biological activity should be provided.

Verification of the removal or dilution of product-related and non-product related impurities, e.g. processing reagents, endotoxin contaminating cell proteins or nucleic acids, and other residual contaminants should be included. A standard denominator (e.g. international units) should be used to facilitate comparison through processing, concentration, or dilution. If the purified substance is

held prior to further processing, a description of the storage conditions and time limits should be included.

(e) Stabilization process (if applicable)

A description should be provided for any post-purification steps performed to produce a stabilized immunogenic substance (e.g. adsorption, the addition of stabilizers, the addition of preservatives), and the objectives and rationale for performing each process.

A description of precautions taken to monitor bio-burden and prevent contamination during these processes should also be provided. If the substance is held prior to further processing, a description of storage conditions and time limits should be included. Verification of the stability of the active immunogenic substance under the conditions described should be provided.

(f) Provide the criteria for pooling more than one batch (if applicable)

The details on reuse and/or regeneration of columns and adsorbents and monitoring for residual impurities and leachable reagents should be provided.

Depending on the source of the immunogenic substance, other details about the manufacturing process are provided in module 3.

3.2. S.3. Manufacturing Consistency

Consistency of the manufacturing process for each immunogenic substance component should be demonstrated by providing the manufacturing lot certificates of at least three, preferably consecutive, batches of the active immunogenic substance of a size corresponding to that for routine production. The establishment and use of the reference standards in assuring consistency in product characteristics.

3.2. S.4. Reference standards or materials

The establishment and use of reference standards or materials in assuring consistency in product characteristics should be described. Information under this section should include a description of the preparation, characterization, and stability of primary and working reference standards.

A detailed description of the procedures to qualify new lots of reference standards and acceptance criteria for a new reference standard should be included. Certificate(s) of analysis of reference standard or materials used should also be provided.

3.2. S.5. Container and Closure System

A description of the container and closure system and information on its compatibility with the immunogenic substance should be provided.

Detailed information concerning the supplier, address, and the results of compatibility, toxicity, and biological tests should be included. If the immunogenic substance is intended to be sterile,

evidence of container and closure integrity for the duration of the proposed shelf life should be provided.

3.2. S.6. Stability of immunogenic substance

This section should contain information on the stability of the immunogenic substance and any in-process material at each holding step. At least stability data from three consecutive batches should be provided.

3.2.S.6.1 Protocol of stability study, summary, and conclusions

The stability protocol which includes all the storage conditions (temperature, humidity, light) in which the immunogenic substance is evaluated should be provided.

3.2.S.6.2 Stability data

Stability data should be provided for at least three representative consecutive batches stored in the final container.

3.2.S.6.3 Storage and shipping conditions of immunogenic substance

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

3.2.P Immunological Veterinary Product (IVP)

3.2. P.1 Description and Composition of the IVP

Information provided should include:

3.2.P.1.1 Description of the dosage form

In this section, a clear description of the IVP and packaging materials should be provided.

3.2.P.1.2 Qualitative and Quantitative Particulars.

A tabulated list of all components of the immunological veterinary product and diluents (if applicable) should be given as per table 1 below. The quantities per dose should be stated. A clear description of the active immunogenic substance including the name(s) or designation of the strain of organism used to produce the active immunogenic substance should be provided.

The reason(s) for the inclusion of each excipient, reference standard, and a justification for overages should also be stated.

Where applicable, special characteristics of excipients should be indicated. The type of water (e.g. purified, demineralized), where relevant, should be indicated.

Table 1: Composition of the Immunological Veterinary Product

1. Active (immunogenic) ingredients

Name	**Function/reason for inclusion**	**Quantity per dosage Unit**	**Specification or reference text**

2. Inactive ingredients (adjuvant/excipients/preservative)

Name	**Function/reason for inclusion**	**Quantity per dosage Unit**	**Specification or reference text**

3.3. P.2 Method of manufacture

3.2.P.2.1 Manufacturer

The name(s) and physical address (es) of the manufacturer(s) of the IVP including activities performed at each manufacturing site including contract manufacturers for production and quality control should be stated. The manufacturing authorization and certificates of compliance with GMP requirements should be provided in module 1.

3.2.P.2.2 Flow chart of the manufacturing process

A complete visual representation of the manufacturing process flow should be provided for the immunological veterinary product.
The steps in production, including incubation times and temperatures, equipment and materials used, the areas where the operations are performed and a list of the in-process controls and finished product tests performed at each step should be stated. In-process holding steps should be included with time and temperature limits indicated.

3.2.P.2.3 Description of the manufacturing process

A detailed description of the manufacturing process of the IVP including the sterilization operations, aseptic processing procedures, filling, lyophilization (if applicable), and packaging should be provided. Results of studies validating the compatibility of the components including the adjuvant and/or preservatives, if applicable, should be provided.

3.2.P.2.4 Control of Starting Materials

A list of all starting materials including culture media, buffers, and resins for peptide synthesis, chemicals used in the manufacture of the immunogenic substance, and their specifications or reference to official compendia should be provided.
For purchased starting materials, representative certificates of analysis from the supplier(s) and/or manufacturer's acceptance criteria should be provided.
Monographs of starting materials listed in pharmacopeias and starting materials not listed in a pharmacopeia (description and seed materials for starting materials of biological origin, and description and identification of starting material of non-biological origin).

The following in-house preparation of media should be described:
(a) Starting material listed in pharmacopeias;
(b) Starting materials not listed in pharmacopeias.
    (i) Starting materials of non-biological origin;
    (ii) Starting materials of biological origin.
Details on the control of starting materials of biological origin are provided in module 3.

3.2.P.2.5 Minimising the risk of Transmissible Spongiform Encephalopathy (TSE)

The carry-over of impurities of the starting materials for synthesis into the final immunogenic substance should be considered and discussed.

A letter of attestation should be provided confirming that the active substance, the starting materials, and reagents used to manufacture the immunogenic substance are without risk of transmitting agents of animal spongiform encephalopathies.

When available, a CEP demonstrating TSE-compliance should be provided. A complete copy of the CEP (including any annexes) should be provided in Module1.

3.2.P.2.6 Media preparation

Details of methods of preparation and sterilization of all media must be provided. Culture media must be stored at the specified temperature, under specified conditions, and for no longer than the

applicable shelf life. Quality control tests should be carried out to ensure that the performance characteristics of the medium are within specification.

3.2.P.2.7 In-process control tests

A description of all analytical testing performed to characterize the active immunogenic substance with respect to identity, quantity, and stability with their test results should be presented in either tabular form, legible copies of chromatograms or spectra, photographs of gels or immunoblots, actual histograms of cytometric analysis or other appropriate formats.

The report should also include a brief description of sampling procedures and test methods. Data should be well organized and fully indexed to enable easy access. Results for quantitative assays should be presented as actual data not generally as “Pass” or “Fail”.

For any process, which is not intended to be sterile, documentation of the control of extraneous bioburden by a tabulation of in- process testing for bioburden should be provided.

3.2.P.2.8 Process Validation

A complete report, including protocols, results, and control standards used should be provided for the validation studies of each critical process or factor that affects active immunogenic substance specifications. The validation study reports that have been subjected to statistical rigor should demonstrate the variability in each process as it relates to final specifications and quality. The characteristics of specific antibodies used in the immunochemical or serological assays should also be included.

3.2.P.3 Control Tests on the Finished Product

3.2.P.3.1 Specifications

Detailed information on finished product tests performed on each batch, including the batch release specification, must be provided. The following information should be provided:

(a) Appearance

A qualitative statement describing the physical state (lyophilized solid, powder, liquid) and color and clarity of the Immunological Veterinary Product.

(b) Identity

The method used to establish the identity of the IVP, including the identification of the active substance(s) should be described. The description should include an evaluation of the specificity and sensitivity of the method.

(c) Purity/sterility

Include information on the purity or sterility of the Immunological Veterinary Product.

(d) Safety

If available, provide results of the batch safety tests performed in the target animal species. (EMA reference) If available.

(e) Potency/Titer

A description of the potency assay for the Immunological Veterinary Product should be provided. Information should be submitted on the sensitivity, specificity, and variability of the assay including the data from the material used to prepare clinical lots which were used to set the acceptance limits for the assay.

(f) Chemical and Physical tests

Provide information on the chemical and physical tests carried out on the finished Immunological veterinary product. These shall include: pH and, if applicable, adjuvant, preservative, residual humidity, viscosity, emulsion, residual inactivate, etc.

(g) Sampling procedures

The sampling procedures for monitoring a batch of an immunological veterinary product should be included.

3.2.P.3.2 Analytical methods

A description of all test methods selected to assure the identity, purity, titer/or potency, as well as the lot-to-lot consistency of the finished product and the specifications used for the immunogenic product should be submitted.

3.2.P.3.3 Validation of analytical methods

The results of studies validating the specificity, sensitivity, and variability of each method used for release testing should be provided. Where applicable this should include descriptions of reference standards and their validation. For analytical methods in compendial sources, the appropriate citations should be provided.

3.2.P.4 Batch to batch consistency

Provide at least three consecutive production batches of the immunological veterinary product of a size corresponding to that for routine production. Results from the three consecutive batches should be provided in tabular form for ease of comparison. Certificates of analysis of each batch should be provided. The manufacturing records of these three batches should be provided.

3.2.P.5 Containers

Details of the container and closure system and its compatibility with the immunological veterinary product should be submitted. Detailed information concerning the supplier(s), address (es), and the results of any relevant information on compatibility, toxicity, and biological tests should also be provided for containers of novel origin.

For sterile products, evidence of container and closure integrity should be provided for the duration of the proposed shelf life.
Container closure system - specifications including descriptions and identification of primary packaging components should be provided.

3.2.P.6 Stability of the Final Immunological Veterinary Product

Evidence should be provided to demonstrate that the product is stable for the proposed shelf-life period under the storage conditions described on the label. The ultimate proposed shelf life should be stated.

3.2.P.6.1 Protocol of stability study, summary, and conclusions

Stability protocol and data should be provided for at least three representative consecutive batches stored in the final container. The three consecutive production runs may be carried out on a pilot scale (10% of full scale), providing this mimics the full-scale production method described in the application, or manufacturing scale (the largest scale validated and proposed for registration for commercial use).

The storage temperature should be stated together with the results of tests on the batches. A plan for on-going stability studies should be provided indicating the batch numbers of the batches on test and the time points when testing is planned.

Examples of stability-indicating tests to be performed:

(a) Sterility at time zero and end of shelf life;
(b) Potency/virus titer/bacterial counts;
(c) Physical and chemical tests, as appropriate, such as:
    (i) Moisture content of lyophilized vaccines (VICH GL26);
    (ii) Tests to quantify the adjuvant;
    (iii) Oil adjuvanted vaccine should be tested for viscosity by a suitable method;
    (iv) The stability of the emulsion should be demonstrated;
    (v) Quantitative assay of any preservatives.

For multi-dose presentations, when a preservative is included in the vaccine, preservative efficacy should also be studied at the minimum and maximum time points as defined in Ph. Eur.5.1.3 and at the lower preservative limit at the end of shelf-life specification if there is a range.
Note: A preservative may only be included in a single dose vial if it can be shown that the single-dose vial is filled from the same bulk blended vaccine as a multi-dose container.
The pH of liquid products and diluents should be measured and shown to be within the limits set for the product.
Target animal safety testing: for conventional vaccines, it may be acceptable to omit the target animal safety test at each shelf life testing point.

The shelf life starts at the time of the first titration (live vaccines) or potency test. For example, for in vivo potency tests, the shelf life starts from the date of the first administration of the vaccine to the species in which the potency test is carried out.

For vaccines stored by the manufacturer at a temperature lower than that stated on the label, the stability for the entire storage period should be demonstrated. The expiry date is then calculated from the date that the vaccine is stored under the conditions stated on the label.

3.2.P.6.2 In-use shelf life

Stability-indicating tests should be provided on at least 2 different batches to support an in-use shelf life. Target animal safety testing is not normally required.

(a) After first opening the container:

Generally, an in-use shelf life after the first opening should not exceed 8-10 hrs.
For live vaccines an in-use shelf life of 8-10 hours must be supported by virus/bacterial titration data. For inactivated vaccines omission of the potency test at the end of the in-use shelf life can be justified if the potency test is an in-vivo test.

(b) Shelf-life after dilution or reconstitution:

The shelf life after reconstitution according to the directions should not exceed 10 hours. The product must be reconstituted with the approved diluents and in line with the recommendations. The shelf life after reconstitution must be supported by virus/bacterial titration or potency data.

No losses of titer or potency should be observed. For inactivated vaccines omission of the potency test at the end of the in- use shelf life can be justified if the potency test is an in-vivo test.

(c) Extended in-use shelf life:

A CMPV guideline (EMEA/CVMP/IWP/250147/2008) on data requirements to support in-use stability claims for veterinary vaccines is available https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-data-requirements-support-use-stability-claims-veterinary-vaccines_en.pdf.

The guideline places emphasis on conducting the in-use stability study mimicking the conditions of use of the vaccine in the field.

Note: For guidance on "Stability testing of Biotechnological Veterinary Medicinal Products" refer to VICH GL 17 (CVMP/VICH/501/99) found at https://www.ema.europa.eu/en/documents/scientific-guideline/vich-gl17-stability-testing-biotechnological/biological-veterinary-medicinal-products-step-7_en.pdf

3.2.P.6.3 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.

3.2. D. MANUFACTURING AND CONTROLS OF RECONSTITUTION DILUENTS

For any immunological veterinary product accompanied with reconstitution diluents, the following data should be submitted for diluents(s):

(a) Name of reconstitution diluents(s);
(b) Name and physical address of the manufacturer, telephone, and e-mail of the reconstitution diluents(s);
(c) Valid Certificate of Good Manufacturing Practice and Valid Manufacturing Authorization for the production of the diluent(s) should be provided in module 1;
(d) Description of the reconstitution diluents(s);
(e) Qualitative and Quantitative particulars;
A tabulated list of all components of the diluents (if applicable) should be given as per table 4 below. Name of diluents, Quantity per dosage unit, and the reason(s) for inclusion of each excipient (if applicable) should be stated;

Name	**Quantity per Unit dosage**	**Quantity per batch**	**Specifications/ Reference text**	**Reasons for inclusion**

(f) Specification of reconstitution diluents(s) along with certificates of analysis;
(g) Description of manufacturing method production and control of starting materials;
(h) Control tests during the manufacturing process;

(i) Compatibility studies with reconstitution diluents to support claims in the label. The compatibility of diluents e.g. precipitation of IVP in solution, sorption on injection vessels, and stability should be addressed to provide appropriate and supportive information for labelling;
(j) Process validation report;
(k) Control tests of the finished product;
(l) Sterility tests;
(m) Analytical validation report;
(n) Specifications of container closure system along with certificates of analysis;
(o) Stability report that includes.
  (i) The study protocol;
  (ii) Specifications;
  (iii) Analytical method;
  (iv) Description of the container closure system for the diluents;
  (v) Storage conditions (temperature and relative humidity);
  (vi) Summary of results for at least three batches of diluents;
  (vii) Proposed validity period;
  (viii) The stability documents should be provided on an officially recognized document, signed by responsible personnel, dated with a version control number.

MODULE 4: SAFETY

Table of contents

1.1 Report on studies

Reports of laboratory tests and field trials performed to demonstrate all aspects of safety of the product during use, together with the conclusions, should be provided.

The reports relating to the laboratory tests and field trials should be written using the sequence of headings below:

(a) Title of the test, with reference number;
(b) Introduction including a statement of the aims of the test study;
(c) Reference to relevant monographs;
(d) Name(s) and business address (es) of key personnel and location of the research institute involved in the study;
(e) Dates of start and end of the test or study;
(f) Summary;
(g) Material and methods;
(h) Results;
(i) Discussion;
(j) Conclusion.

1.2 Laboratory Tests

For guidance on how to design and monitor these studies refer to CVMP/VICH/359665/2005, VICH GL44: "Target animal safety for veterinary live and inactivated vaccines". https://www.ema.europa.eu/en/documents/scientific-guideline/vich-gl44-target-animal-safety-veterinary-live-inactived-vaccines-step-7_en.pdf.

4.1.4.1 Single-dose toxicity studies

The immunological veterinary product should be administered at the recommended dosage and by the recommended route of administration to each species in which it is intended to be used. The animals should be monitored daily for 14 days, observing and recording objective criteria such as rectal temperature, injection site reaction, and effect on performance.

4.1.4.2 Overdose toxicity studies

The immunological veterinary product should be administered at an overdose (normally 10 times the recommended dose for live vaccines and 2 times for inactivated vaccines) by the recommended route of administration to each species in which it is intended to be used. The animals should be monitored daily for 14 days, observing and recording objective criteria such as rectal temperature, injection site reaction, and effect on performance.

4.1.4.3 Repeated dose toxicity studies

The immunological veterinary product should be shown to be safe by considering the number of doses that are likely to be used by the animal during its lifetime.
For example, if the vaccination schedule requires a 2-dose primary course followed by a single annual booster, the repeated administration test should consist of 3 separate doses.
The doses may be given 2 weeks apart by the recommended route of administration to each species in which it is intended to be used. This study may be run in conjunction with the single-dose study.

The animals should be monitored daily for 14 days after each administration, observing and recording objective criteria such as rectal temperature, injection site reaction, and effect on performance.

4.1.4.4 Safety studies for live attenuated vaccines

(a) Spread of the vaccine strain;
(b) Shedding and spread of the vaccine strain from vaccinated to unvaccinated animals should be studied and assess the implications of the results should be reported;
(c) Dissemination in the vaccinated animal;

(d) Studies to demonstrate if the vaccine strain is present in animal secretions or the tissues of the vaccinated animal should be conducted;
(e) Safety of a live, attenuated vaccine from Reversion to Virulence;
(f) These studies should be conducted according to the following guidance CVMP/VICH/1052/2004, VICH GL41: "Target animal safety: Examination of live veterinary vaccines in target animals for the absence of reversion to virulence." https://www.ema.europa.eu/en/documents/scientific-guideline/vich-gl41-target-animal-safety-examination-live-veterinary-vaccines-target-animals-absence-reversion_en.pdf
(g) Recombination or genomic re-assortment of strains;
(h) Discussion should be provided on the probability of recombination or genomic re-assortment with field or other strains.

4.1.4.5 Field Safety

The safety of the immunological veterinary product should be evaluated during field trials. Both safety and efficacy may be assessed during the same trial. Batches used in the trials must be manufactured according to the method described in Module 3.

4.1.4.6 Other Safety Issues to be considered

(a) Safety to the user:
For specific guidance on safety to the user reference should be made to CVMP/54533/06, adopted guideline: "User safety for immunological veterinary products".

(b) to the environment:
For specific guidance on safety to the environment, reference should be made to CVMP/074/95 "Environmental risk assessment for immunological veterinary products".

(c) Safety of residues:
For food-producing animals, the effects of residues of constituents of the vaccine such as adjuvants or live zoonotic organisms used as antigens should be considered. A suitable withdrawal period should be provided.

(d) Interactions:
The safety of administering the immunological veterinary product at the same time or the same site as another immunological veterinary medicinal product must be demonstrated if a recommendation for such use is to be made on the SmPC.
For specific guidance on the safety for combined vaccines and associations of immunological veterinary medicinal products reference should be made to CVMP/IWP/594618/2010, "Requirements for combined vaccines and associations of immunological veterinary medicinal products (IVMPs)".

MODULE 5: EFFICACY

5.1. Table of contents

5.2. Efficacy studies Reports

Particular tests in the target species of animal to demonstrate the efficacy of the IVP to support the indications for which it will be used should be provided. Details of the following studies should be provided.

5.2.1. Laboratory Efficacy

5.2.1.1. Controlled clinical studies on efficacy (Immunological Veterinary Products-challenge studies)

Evidence of efficacy under reproducible controlled conditions should be provided. Efficacy should normally be demonstrated by administering a challenge infection with a heterologous strain. If protection against challenge infection has been shown to correlate with serology it may be possible to demonstrate efficacy by serological methods. The batch (es) used in laboratory efficacy studies should be manufactured and tested according to the methods described in Module 3 and contain the minimum quantity of antigen permitted for batch release. It should be administered to the target species at the recommended dose by the recommended route of administration.

5.2.1.2. Compatibility studies

Where relevant data should be provided on the following studies:

(a) Studies on potential beneficial interactions with other IVP administered at the same time;
(b) Studies on the potential decrease in efficacy when administered at the same time as other IVP (interference).

Each individual study report should include the following information:

(a) Identity and qualifications of key personnel involved;
(b) Location(s) of study;
(c) Date(s) of study;
(d) Study design;
(e) Selection of animals (inclusion, exclusion criteria);
(f) Selection of controls;
(g) Selection of control treatment (if applicable);
(h) Number of animals involved;
(i) Response variables endpoints;
(j) Details on randomization, blinding, compliance, and justification;

(k) Treatments given identity and quality of the investigational and control products used, the dosage used, duration of treatment, duration of observation periods, any concurrent treatments, and their justification;
(l) Analytical methods for determining antibodies if serology is applicable as a measure of efficacy;
(m) Analysis of results including statistical analysis;
(n) The proposed indication(s) of the product should be stated;
(o) Discussions and conclusions on efficacy and safety;

5.2.2. Field Efficacy

The immunological veterinary product should be tested in controlled field trials. The batch (es) used in field trials should be manufactured and tested according to the methods described in module 3. It should be administered to the target species at the recommended dose by the recommended route of administration. For specific guidance on conducting field efficacy trials reference should be made to EMA/CVMP/852/99, "Field trials with veterinary vaccines".

ENDORSEMENT OF THE GUIDELINES

	Prepared by	**Checked by**		**Approved by**
Title	**Division manager**	**Head of Department**	**QMS Division Manager**	**Director General**
Names	Dr. Doreen INGABIRE	Dr. Védaste HABYALIMANA	Ms. Marie Ange UWASE	Prof. Emile BIENVENU
Signature & Date	Digitally signed by RWANDA FDA(Division Manager VMDR) Date: 2025.08.18 08:34:50 +03'00'	Digitally signed by RWANDA FDA(Head of Drugs Department) Date: 2025.08.20 16:18:54 +02'00'	Digitally signed by Marie Ange UWASE Date: 2025.08.21 11:31:50 +02'00'	Digitally signed by RWANDA FDA(Director General) Date: 2025.08.26 09:29:12 +02'00'

ANNEXES

Annex 1: Cover Letter
Annex 2: Application Form
Annex 3: Quality Overall Summary (QOS)
Annex 4: Summary of Product Characteristics (SmPC)
Annex 5: Container Labeling
Annex 6: Product Information Leaflet (PIL)
Annex 7: Marketing Authorization Certificate

Note: The annexes mentioned above are available on the Rwanda FDA website, under Veterinary Medicines Registration.