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| --- |
| **APPLICATION FOR REGISTRATION OF A VETERINARY MEDICINE**  |

**ADMINISTRATIVE DATA** **APPLICATION NUMBER**

|  |
| --- |
|  |

PART 1 A.

(a) PARTICULARS OF APPLICANT / PROSPECTIVE HOLDER OF THE CERTIFICATE OF REGISTRATION (PHCR)

|  |
| --- |
| Name: Business address: Postal address: Telephone No: Fax No: E-Mail address: Site/Applicant Master File Number: Person responsible/ authorised to communicate with AuthorityName: -----------------------------------------------------------------------------------------------------Business address: --------------------------------------------------------------------------------------Telephone no: -------------------------------------------------------------------------------------------Fax No.: ---------------------------------------------------------------------------------------------------E-mail: -----------------------------------------------------------------------------------------------------***(Attach a letter of authorisation signed by the Managing Director/Chief Executive Officer)*** |

(b) PARTICULARS OF THE VETERINARY MEDICINE

|  |
| --- |
| Proprietary name: Pharmacological Classification: -------------------------------------------Dosage form: Active pharmaceutical ingredient(s) and strength(s) per dosage unit: Indicate with an X in the appropriate block if the application is for a New product with new active  new product with existing active  Amendment to existing product. Registration no.   Parallel product  daughter product  multi – source product  veterinary biologicalRoute of administration: Pharmacological classification: Manufacturer: Business address: Site Master File reference number:  Packer: Business address: Site Master File reference number: Final product release control (FPRC): Business address: Site Master File reference number: Final product release responsibility (FPRR): Business address: -----------------------------------------------------------------------------Site/Applicant Master File number( s) : ----------------------------------------------------------------------- |

**The undersigned hereby declares that all the information herein and in the PARTs hereto are correct and true and are relevant to this particular medicine.**

..................................................................

Signature of Responsible Person

................................................................... .......................................................................

Name in block letter Date of application

...................................................................

Designation .......................................................................

............................................................. Date of current amendment

(c) UPDATE HISTORY (**For Variations Only**)

| **LETTER DATE OF APPLICATION FOR VARIATIONS** | **SUMMARISED DETAILS OF VARIATIONS** | **DATE OF APPROVAL BY AUTHORITY** |
| --- | --- | --- |
|  |  |  |
|  |  |  |
|  |  |  |

**PART 1B COMPREHENSIVE TABLE OF CONTENTS**

A comprehensive table of contents of the dossier, including the Sub – PARTs of each PART, shall be provided

## PART 1 C LABELLING

 **(a) PARTICULARS OF THE VETERINARY MEDICINE**

 **SCIENTIFIC PROFFESSIONAL INFORMATION**

The under-mentioned information with regard to this medicine shall appear on the scientific package insert. The information shall be presented in the format stipulated: Provided that the Authority may authorise any deviation from such information or such format (refer to Regulation 40).

1. The words “**Veterinary Medicine**”
2. Scheduling status
3. Proprietary name and dosage form
4. Composition
5. Pharmacological classification
6. Pharmacological action

Pharmacokinetics and Pharmacodynamics

1. Indications per species.
2. Contra-indications
3. Warnings and/or withdrawal period in the case of food-producing animals

 Safety in pregnancy and lactation

1. Dosage and directions for use including per age and species dosage
2. Side effects and special precautions for use per species.

 Interactions

1. Known signs of over-dosage and particulars of its treatment per species
2. Identification
3. Presentation
4. Storage instructions
5. Registration number
6. Name and business address of the holder of the certificate of registration
7. Date of notification of approval of this scientific professional information

**PART 1 C (b) SPECIMEN OF THE LABEL**

A specimen of the immediate container label and, if applicable, the outer label shall be included here. This shall conform to Regulation 48.

PART 1 D FOREIGN REGISTRATION

a) A list of countries in which an application has been lodged and the status of these applications shall be furnished, detailing approvals, deferrals, withdrawals and rejections.

b) If the medicine has been registered by the regulatory authorities with which Authority aligns itself, i.e.
Members and Observers of the VICH: USA (FDA), European Union (EMA), UK (VMD), Japan (JMAFF), Health Canada (VDD), Australia (APVMA) and New Zealand.

* a copy of the certificate of registration
* the conditions of registration and
* the approved professional information (data sheet) translated into English.

c) Details of any negative decision by any regulatory authority reflected in PART 1D b) shall be provided. PART 2 BIOEQUIVALENCE AND BIOAVAILABILTY

**a) STATE THE PURPOSE OF THE STUDY**

(i) As comparison of formulation to be marketed versus formulation used in clinical trials, or

(ii) As proof of efficacy for a multi - source application, or

(iii) As proof of efficacy of new formulation (formulation change)

**(b) REFERENCE PRODUCT USED**

(i) Clinical trial formulation

(ii) Innovator product

(iii) Current formulation (for change of formulation)

The following must be indicated:

|  |  |  |
| --- | --- | --- |
|  | **Reference Product** | **Formulation Applied For** |
| Name of product |  |  |
| Batch no |  |  |
| Holder of certificate of registration  |  |  |
| Country where purchased |  |  |
| Assay results |  |  |
| Source of Active Pharmaceutical Ingredient |  |  |

**(c) METHOD USED**

Describe the method in full, e.g. bioavailability, dissolution, etc.

**(d) VALIDATION**

Validation data for all quantitative assay methods shall be included.

1. **STUDIES**

Include protocol, final report, assay validation report, pharmacokinetic report (including individual animal data) and statistical report.

**(f) DISCUSSION AND CONCLUSION**

Attach documents (where applicable)

*Partial or total exemption from the requirements of this Part may be applicable if efficacy and safety are intended to be established by clinical data (or for other reasons determined by Authority) , provided that clinical trials have been conducted with the same formulation as the one being applied for .*

**PART 3**

**QUALITY CONTROL**

**PART 3A (i) VETERINARY PHARMACEUTICAL MEDICINES**

 **ACTIVE PHARMACEUTICAL INGREDIENT REQUIREMENTS (DEVELOPMENT CHEMISTRY AND CHARACTERISATION)**

a) The name(s), structural formulae, empirical formulae, molecular mass, solubility and storage requirements are as follows:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| International Nonproprietary Name (INN) or approved name and chemical name | Structural formula, empirical formula, molecular mass | Solubility | Storage requirements | Re – test period |
|  |  |  |  |  |

b) The active pharmaceutical ingredient(s) [ API] are obtained from the following sources:

 Stipulate names and business addresses of the manufacturer(s)

c) Active Pharmaceutical Ingredient File (APIF) or Drug Master File [DMF] (open part) or certificate of suitability (CEP) shall be included.

1. Certificate of analysis of two batches
2. Proof of physical and chemical equivalence (more than one manufacturer)

f) Stability data and shelf-life of active pharmaceutical ingredient

**PART 3A (ii) VETERINARY BIOLOGICALS**

**PRIMARY PRODUCTION LOT/BATCH**

**1. DESCRIPTION OF THE PREPARATION AND PRODUCTION OF THE PRIMARY PRODUCTION LOT.**

a) Name and address of the manufacturing facility in which production of the primary production lot takes place.

b) Master seed Identification, description and control

c) The complete description of the preparation and manufacturing process of the primary production or bulk lot, the tests carried out on the product and the stages at which such tests are carried out to confirm the integrity of the product must be submitted.

**2. SPECIFICATIONS OF INGREDIENTS USED IN THE PRIMARY PRODUCTION LOT**

 The following are the specifications that apply to the ingredients used in the primary production or bulk lot of a veterinary biological medicine, including the titles of the tests and the limits and criteria of acceptance of each parameter contained in the specification. (Where the test mentioned corresponds to a recognised pharmacopoeia, the source shall be mentioned):

**3. TESTS CARRIED OUT ON INGREDIENTS IN THE PRIMARY PRODUCTION LOT AND DETAILS OF THE LABORATORIES INVOLVED**

 The following is a complete description of the tests carried out on all the ingredients used in the primary production or bulk lot, specifying the name and address of the laboratory (ies) in which such tests are carried out.

**PART 3 B (i) FORMULATION**

**FORMULATION OF THE FINAL DOSAGE FORM**

a) Below is a schedule of the names and quantities of each active and inactive ingredient contained in a dosage unit. Where no dosage unit exists, other suitable unit of mass or volume of the veterinary medicine may be used and these shall conform to the relevant particulars in the package insert and on the label with regard to the active pharmaceutical ingredients.

b) The purpose(s) of each inactive ingredient in the formulation shall be specified, including that of raw materials used in manufacturing, but which are not present in the final product.

|  |  |  |  |
| --- | --- | --- | --- |
| **Approved name**  | **Quantity per dosage unit\*** | **Active or inactive** | **Purpose of inactive** |
|  |  |  |  |

\*mg per tablet/capsule/lozenge/suppository or mg or ml per specified volume or mass of product

c) Potency calculations. A statement to the effect that the actual quantity of the active pharmaceutical ingredient will depend on the potency shall be included.

d) Composition of inactive ingredients in combination, mixtures, etc.

e) Overages and justification for their inclusion.

f) Toxicity level per dosage unit must be indicated for all solvents and for other ingredients when required by Authority. Levels must be indicated as per “USP DI” or “Martindale”, or “The Complete Drug Reference”, or other specified reference.

**PART 3 B (ii) FORMULATION OF THE FINAL FILLING LOT FOR VETERINARY BIOLOGICALS**

a) Below is a schedule of the names and the strength or concentration of each active and inactive in the veterinary biological and with regard to the active ingredients, conform to the relevant particulars in the package insert and on the label.

b) The purpose of each ingredient in the formulation shall be specified, and raw materials used, even if not present in the final dosage form but used during manufacture, shall be mentioned.

|  |  |  |  |
| --- | --- | --- | --- |
| **Approved name or chemical name of constituent** | **Quantity per unit \*** | **Purpose** | **Purpose of inactive** |
|  |  |  |  |

 \*%m/m,m/v,v/v

**SECTION 3B (iii)**

**FORMULATION OF THE RECONSTITUTING LIQUID FOR THE FINAL FILLING LOT FOR BIOLOGICAL VETERINARY MEDICINES**

(a) Below is a schedule of the names and quantities of each ingredient contained in the diluent.

1. The purpose of each ingredient in the formulation shall be specified, and raw materials used, even if not present in the final diluent shall also be given.

|  |  |  |
| --- | --- | --- |
|  Approved name or chemical name of constituent | Quantity | Purpose |
|  |  |  |

###### **PART 3C SPECIFICATIONS AND CONTROL PROCEDURES**

**FOR RAW MATERIALS USED IN THE MANUFACTURE OF THE FINAL PRODUCT (VETERINARY MEDICINES) OR FINAL FILLING LOT AND DILUENTS (VETERINARY BIOLOGICALS )**

a) Pharmacopoeial ingredients.

|  |  |  |  |
| --- | --- | --- | --- |
| **Pharmaceutical Ingredient** | **Specifications and Pharmacopoeial reference\*** | **Limits** | **Additional Tests (e.g. particle size)** |
| Active |  |  |  |  |
| Inactive |  |  |  |  |

 \*The latest edition of the pharmacopoeia is implied, unless otherwise specified and justified.

(b) Non-pharmacopoeial ingredients. In – house specifications and control procedures for these ingredients should be included.

|  |  |  |  |
| --- | --- | --- | --- |
| **Pharmaceutical Ingredient** | **Specifications**  | **Limits** | **In-house control procedures** |
| Active |  |  |  |  |
| Inactive |  |  |  |  |

c) The applicant must comply with and confirm the following requirements in the application:

(i) Identification and assay of the active raw material, irrespective of the possession of a certificate of analysis from the supplier.

(ii) Identification of the inactive raw material, irrespective of the possession of a certificate of analysis from the supplier.

(iii) Perform any other tests not included in a valid certificate of analysis.

d) The frequency of testing of water, where applicable, must be included.

**PART 3 D CONTAINER AND PACKAGING MATERIAL**

**a) DESCRIPTION OF CONTAINERS**

 (i) Immediate container, including any patient-ready packs, closure, wadding, desiccant (type of material and dimensions, including sketches).

1. Outer container (type of material of container).
2. Bulk container (type of material of container).
3. Application and administrative sets (type of material and dimensions

 including sketches).

**b) SPECIFICATIONS AND LIMITS FOR PACKAGING MATERIALS**

 **The following must be completed:**

|  |  |  |
| --- | --- | --- |
| Specification | Limit | Name of manufacturer/packer of the final product |
|  |  |  |

 Indicate those tests performed by the supplier of the packaging material.

**c) DESCRIPTION OF CONTROL PROCEDURES PERFORMED BY MANUFACTURER/PACKER OF FINAL PRODUCT**

**d) PACK SIZES**

**PART 3 E MANUFACTURING PROCEDURES**

**Veterinary medicine: manufacturing procedures of final product**

**Veterinary Biological: final filling lot and diluent**

The comprehensive procedure of manufacture, detailing the

* various stages of manufacture
* packaging procedure,
* batch manufacturing formulations(s) and batch size(s),
* in-process control procedures and the frequency with which they are carried out during the manufacturing and packaging process, and the
* names and addresses of the different manufacturing and packaging facilities/sites where the various stages of manufacturing and packaging are carried out if more than one site is involved, are as follows:

**PART 3 F VETERINARY PHARMACEUTICAL FINISHED PRODUCT**

####  VETERINARY BIOLOGICAL FINAL FILLING LOT AND DILUENT

**a) SPECIFICATIONS AND LIMITS**

The following tables include the specifications, limits criteria for acceptance of all physical , chemical and , where applicable , microbiological parameters and the responsible laboratories for :

(i) in - process control

|  |  |  |
| --- | --- | --- |
| Specification | Limits | Responsible Laboratory (ies) |
|  |  |  |

 (ii) Final product control

|  |  |  |
| --- | --- | --- |
| Specification | Limits | Responsible Laboratory (ies) |
|  |  |  |

(iii) Stability studies

|  |  |  |
| --- | --- | --- |
| Specification | Limits | Responsible Laboratory (ies) |
|  |  |  |

(iv) Reconstituted/diluted final product

|  |  |  |
| --- | --- | --- |
| Specification | Limits | Responsible Laboratory (ies) |
|  |  |  |

Final product specifications, for imported products upon local receipt the product must be re – identified and assayed, unless a supplier / transport validation has been submitted to and approved by Authority. In all cases a valid Certificate of Analysis which shows all the tests described in the final product specification must accompany the shipment. Should any of the required tests be omitted from the CoA, then these tests must be re – done locally prior to the release.

**b) TABLE OF TESTS TO BE PERFORMED**

|  |  |
| --- | --- |
|  | **TITLE OF SPECIFICATION** |
| FPRC |  |
| FPRC responsible for tests after importation | IdentificationAssay |
| FPRR | Appearance of dosage formContainerPackage insertLabelBatch No.Expiry date.Certificate of AnalysisBatch release documents |

**c) CONTROL PROCEDURES**

Description of the control procedures for all the specifications in section (a) and a final product certificate of analysis must be included

**d) VALIDATION**

Validation data for all quantitative assay methods must be included.

It must be demonstrated that the assay method is stability indicating, i.e. will distinguish between the active ingredient and the degradation product (s ). If the assay method is not stability indicating the validation data of the procedures used to determine the assay and that used to determine the degradation product must be submitted separately.

**PART 3 G STABILITY DATA FOR THE FINISHED PRODUCT**

1. **Stability programme**

Describe the stability programme to be followed and include the following:

(i) Conditions (temperature, humidity)

(ii) Time points of determination, e.g. 0, 3, 6, 9 months, etc.

1. **Discussion and motivation of shelf-life for each type of container**
2. **Stability data**
3. **Stability test control procedures and validation if different to those of the final product.**

##### **PART 3 H PHARMACEUTICAL DEVELOPMENT**

Describe the pharmaceutical development of the product addressing the choice of formulation, ingredients and containers, overages, manufacture, stability and tests carried out during the development clearly identifying the clinical trial formulations.

**PART 3 I EXPERTISE AND PREMISES USED FOR MANUFACTURING OF VETERINARY BIOLOGICALS**

1. **DETAILS RELATING TO THE PREMISES WHERE PRIMARY PRODUCTION IS UNDERTAKEN AND THE STAFF INVOLVED IN THE PRODUCTION AND TESTING OF VETERINARY BIOLOGICALS.**

a) Description of the premises where all procedures involved in the preparation of the primary production or bulk batch is carried out. (A floor plan must be included):

b) Details of other purposes for which the premises are used:

c) Names, qualifications and field and duration of experience of the persons responsible for the manufacture, testing and release of the veterinary biological medicine, in the form of the primary production or bulk lot and the final containers ready for sale:

1. **NAME AND ADDRESS OF FACILITY WHERE THE IMPORTED FINAL FILLING LOT IS STORED**

**PART 4 PRE-CLINICAL STUDIES**

a) Pre-clinical Expert Report

b) The following are Parts obtained and conclusions drawn from tests performed pre-clinically to demonstrate all aspects of the toxicity of the medicine, and to prove the safety of its use, with special reference to:

(i) acute toxicity,

(ii) subacute toxicity studies;

(iii) chronic toxicity studies;

(iv) reproduction toxicity and teratogenicity studies;

(v) carcinogenicity studies;

1. mutagenicity studies; or
2. environmental impact studies for veterinary medicines
3. pharmacokinetics studies:
4. neurological studies
5. other tests to substantiate the safety of the veterinary medicine;

c) The following are Parts obtained and conclusions drawn from tests performed pre – clinically to demonstrate all aspects of the efficacy of the veterinary medicine, with special reference to:

1. The methods and experimental results of and the conclusions drawn from tests performed pre-clinically with reference to the efficacy of the veterinary medicine;
2. the relationship between the tests performed and the purpose for which the veterinary medicine is or will be used, or for which it will be propagated, and
3. the dosage and method of administration of the veterinary medicine, are as follows:

In cases of multi – source products, the MCC may grant exemption from the submission of some or all of the above information.

**PART 5 SAFETY AND EFFICACY**

 a) Expert Report

b) The field trials performed on target species with regard to the safety of the use of the veterinary medicine, with special reference to the particular dosage, routes of administration used and the side-effects observed per species.

c) Particulars of clinical or field trials conducted to establish the efficacy of the use of the veterinary medicine,

d) Experimental details and results of the studies performed to establish the correlation between the applicable blood and other suitable physiological concentrations and the pharmacological action claimed for the veterinary medicine are as follows:

e) Veterinary medicines for food – producing animals: Residue depletion studies and recommended withdrawal periods

In cases of multi – source products, the Authority may grant exemption from the submission of some or all of the above information as laid down in the guidelines for the registration of these products.