ANNEXURE II

NAMIBIA MEDICINES REGULATORY COUNCIL

MINISTRY OF HEALTH AND SOCIAL SERVICES

APPLICATION FOR REGISTRATION OF A MEDICINE

(Regulation 4)

APPLICATION NUMBER

PART 1 ADMINISTRATIVE INFORMATION

PART 1A ADMINISTRATIVE PARTICULARS

(a) Particulars of the 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 Council:

Name: .....

Business address: .....

.....

Telephone no: .....

Fax no: .....

E-mail address : .....

(Attach a letter of authorisation signed by the person responsible for the overall management and control of the business)

(b) Particulars of the medicine

Category: .....

Proprietary name: .....

Pharmacological classification: .....

Dosage form: .....

Approved name: .....

Strength(s) per dosage unit: .....

Descriptive name of Biological medicine: .....

Route of administration: .....

Country of origin (country in which the original development was carried out): .....

Manufacturer(s): .....

Physical address of site(s): .....

Site Master File reference number(s): .....

Packer(s): .....

Physical address of site(s): .....

Site Master File reference number(s): .....

Finished product release control (FPRC)(s): .....

Physical address of site(s): .....

Site Master File reference number(s): .....

Finished product release responsibility (FPRR)(s): .....

Physical address of site(s): .....

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

…….. Signature of pharmacist (if responsible person is not a pharmacist)

..... Name in block letters

.....…… Date of application

..... Designation

……..……..... Date of current amendment (Post registration only**)**

(c) Amendment history (Post-registration only)

Date of letter of amendment application	Summarised details of amendment	Date of Council response

PART 1B TABLE OF CONTENT

A comprehensive table of content of the dossier, including the SUB-PARTS of each PART, must be provided.

PART 1C LABELLING

(a) Package insert

The under-mentioned information with regard to this medicine must appear on the package insert. The information must be presented in the format stipulated, provided that the Council may authorise any deviation from such information or such format (refer to Regulation 12(2)).

1. Scheduling status
2. Proprietary name and dosage form
3. Composition
4. Pharmacological classification
5. Pharmacological action
   (Pharmacokinetics, pharmacodynamics and summary of clinical studies, where applicable)
6. Indications
7. Contra-indications
8. Warnings
9. Interactions
10. Pregnancy and lactation
11. Dosage and directions for use
12. Side effects and special precautions
13. Known symptoms of overdosage and particulars of its treatment
14. Identification
15. Presentation
16. Storage instructions
17. Registration number
18. Name and business address of the holder of the certificate of registration
19. Date of publication of the package insert.

(b) Patient information leaflet

The under-mentioned information with regard to this medicine must appear on the patient information leaflet. The information must be presented in the format stipulated, provided that the Council may authorise any deviation from such information or such format (refer to Regulation 13(2)).

1. Scheduling status
2. Proprietary name and dosage form
3. Composition of the medicine, that is, what this medicine contains
4. Approved indication and use, that is, what this medicine is used for
5. Instruction before taking the medicine
6. Instructions on how to take the medicine
7. Side effects
8. Storage and disposal information
9. Presentation
10. Identification
11. Registration number
12. Name and business address of the holder of the certificate of registration
13. Date of publication of the Patient Information Leaflet.

(c) Label

A facsimile of the immediate container label and, if applicable, the outer label must be included here. This must conform to Regulation 11.

PART 1D FOREIGN REGISTRATION

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

(b) If the medicine has been registered by the regulatory authorities with which Council aligns itself, i.e. RSA (MCC), USA (FDA), European Union (EMEA), UK (MHRA), Sweden (MPA), Canada (Health Canada), Australia (TGA), and Japan (MWH), include -

- a copy of the certificate of registration,
- the conditions of registration and
- the approved package insert (data sheet) translated into English where relevant.

(c) Details of any negative decision by any regulatory authority reflected in PART 1D b) must be provided.

PART 2 BASIS FOR REGISTRATION AND OVERVIEW OF APPLICATION

PART 2A PHARMACEUTICAL AND BIOLOGICAL AVAILABILITY

(a) The following is an overview with special reference to the purpose of the study(ies), the reference product(s) and the overall conclusion.

(b) The methods and experimental details and results of, and the conclusions drawn from studies/tests carried out to confirm the pharmaceutical and/or biological availability are as follows:

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 as determined by the Council), provided that clinical trials have been conducted with the same formulation as the one being applied for.

PART 2B SUMMARY BASIS FOR REGISTRATION APPLICATION (SBRA)

The following is a summary of the core data in support of the clinical safety and efficacy.

In cases concerning well-known active pharmaceutical ingredients, or if non-clinical and clinical overviews are submitted, the Council may grant exemption from the submission of an SBRA.

PART 2C PHARMACEUTICAL EXPERT REPORT (PER)

The following is an independent, objective and encompassing report in light of current scientific knowledge addressing all the quality aspects of the product.

In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of the above report.

PART 2D PRE-CLINICAL EXPERT REPORT (PCER)

The following is an independent, objective and encompassing report in light of current scientific knowledge addressing all the non-clinical aspects of the development of the product and of the relevant aspects referred to in the package insert.

In cases concerning well-known active pharmaceutical ingredients, or if an SBRA is submitted, the Council may grant exemption from the submission of the above report.

PART 2E CLINICAL EXPERT REPORT (CER)

The following is an independent, objective and encompassing report in light of current scientific knowledge on all the clinical aspects of the development of the product and of the relevant aspects referred to in the package insert.

In cases concerning well-known active pharmaceutical ingredients, or if an SBRA is submitted, the Council may grant exemption from the submission of the above report.

PART 3 PHARMACEUTICAL AND ANALYTICAL

PART 3A(i) ACTIVE PHARMACEUTICAL INGREDIENT (API)

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

International Non-Proprietary Name N(INN) or approved name or chemical name/description	Structural formula, empirical formula, molecular mass	Solubility	Storage requirements	Retest period

(b) The API is obtained from the following sources (names and business addresses of the manufacturers):

(c) The API File (APIF) must be included.

PART 3A(ii) BIOLOGICAL MEDICINE: PRIMARY PRODUCTION LOT/BATCH

(a) Description of the preparation and production of the primary production lot

The following is a complete description of the preparation and manufacturing process of the primary

production or bulk lot, the tests performed and the stages at which such tests are performed to confirm its integrity.

The name and address of the manufacturing facility in which the production of the primary production lot takes place must be provided.

(b) Specifications of ingredients used in the primary production lot

The following are the specifications (titles and limits/criteria) that apply to the ingredients used in the primary production or bulk lot.

If the test corresponds to a recognised pharmacopoeia, this must be mentioned.

(c) 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.

The name and address of the laboratory(ies) in which such tests are carried out must be specified.

PART 3B FORMULATION

(a) Pharmaceutical medicine: final dosage form
Biological medicine: final filling lot/batch

Below is a schedule of the names and quantities of each active and inactive pharmaceutical ingredient contained in a dosage unit. If no dosage unit exists, another suitable unit of mass or volume of the medicine may be used as long as the relevant particulars regarding the active pharmaceutical ingredients correspond in the package insert and on the label.

The purpose(s) of each inactive ingredient in the formulation must be specified, including that of those ingredients used during manufacturing but which are not present in the final product.

Approved name	Quantity per dosage unit	Active or inactive	Purpose of inactive

(b) Pharmaceutical medicine: diluent (if applicable)
Biological medicine: final filling lot reconstituting liquid/diluent

Below is a schedule of the names and quantities of each pharmaceutical ingredient contained in a dosage unit.

The purpose of each ingredient must be specified, including those used but which are not present.

Approved name	Quantity	Purpose

PART 3C SPECIFICATIONS AND CONTROL PROCEDURES FOR PHARMACEUTICAL INGREDIENTS

(a) Pharmacopoeial ingredients

Pharmaceutical Ingredient		Pharmacopoeial reference*	Any additional specifications (e.g. particle size)	Any additional control procedures
Active				
Inactive				

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

(b) Non-pharmacopoeial ingredients

Pharmaceutical Ingredient		Title of Specification	Limits	Control procedures
Active				
Inactive				

(c) Laboratory

The identification and assay of the API and identification of the inactive pharmaceutical ingredients (IPIs) are tested by the following laboratory (name and business address of the laboratory).

PART 3D CONTAINERS AND PACKAGING MATERIALS

(a) Immediate container

The following is a description of the immediate container(s), the nature of the material, closure, pack sizes, specifications and the control procedures performed by the manufacturer/packer of the final product. The tests performed by the supplier are indicated.

(b) Outer container

The following is a brief description of the outer container.

(c) Bulk container

The following is a brief description of the bulk container.

(d) Applicator and administration sets

The following is a description of the applicator and administration sets (if applicable), the type of material and dimensions including sketches.

PART 3E MANUFACTURING PROCEDURE

Pharmaceutical medicine: manufacturing procedures of final product
Biological medicine: 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
- 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 3F FINAL PRODUCT SPECIFICATIONS AND CONTROL

Pharmaceutical medicine: **final product**
Biological medicine: **final filling lot and diluent**

(a) Specifications (titles and limits)

List the specifications (titles and limits) for the following, if applicable:

(i) In-process control.
(ii) Final product control.
(iii) Stability testing.
(iv) Reconstituted/diluted final product.

Title of Specification	Limits

(b) Control

	Final release criteria
FPRC	
FPRR	

(c) Control procedures and validation

The control procedures for the specifications and validation of the analytical assay methods in section (a) and a final product certificate of analysis are included.

PART 3G STABILITY DATA FOR THE FINISHED PHARMACEUTICAL PRODUCT (FPP)

(a) 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.

(b) Discussion and motivation of shelf-life for each type of container

(c) Stability data

(d) Stability test control procedures and validation if different to those of the final product.

PART 3H PHARMACEUTICAL DEVELOPMENT

The following is a description of 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 3I EXPERTISE AND PREMISES USED FOR THE MANUFACTURE OF A BIOLOGICAL MEDICINE

(a) Details relating to the premises where the primary production is undertaken and the staff involved in the production and testing of biological medicines

(b) Name and address of the facility where the final filling lot is stored if imported and/or different to that given in (a).

PART 4 PRE-CLINICAL STUDIES

(a) Pre-clinical Expert Report

(b) The following are results 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;
(vi) mutagenicity studies; or
(vii) other tests to substantiate the safety of the medicine; and
(viii) pharmacokinetic studies.

(c) The methods and experimental results of, and the conclusions drawn from tests performed pre-clinically with reference to the efficacy of the medicine, with special emphasis on the relationship between the tests performed and the purpose for which the medicine is, or will be used or for which it will be propagated, and further, with regard to the dosage and method of administration of the medicine, are as follows:

In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of some or all of the above information.

PART 5 CLINICAL STUDIES

(a) Clinical Expert Report

(b) The clinical trials performed on human volunteers and patients with regard to the safety of the medicine, with special reference to the particular dosage, routes of administration and the side effects observed, are as follows:

(c) The particulars of clinical trials conducted to establish the efficacy of the medicine are as follows:

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

(e) Periodic Safety Update Report for medicines for human use

In cases concerning well-known active pharmaceutical ingredients, the Council may grant exemption from the submission of some or all of the above information.