GUIDELINES FOR RENEWAL OF REGISTRATION OF MEDICINES IN SRI LANKA

1. INTRODUCTION

A marketing authorization for medicines is valid for a maximum period of five year and may be renewed after five years of full registration. This document "Guidelines for Renewal of Registration of Medicines" will serve as the reference guide for the renewal of registration process of medicines.

This documentation shall be read in conjunction with the current laws and regulations controlling medicines in Sri Lanka. The written laws shall take precedence over this guidance document in any event of discrepancy.

The scope of this document includes information relating to administrative requirements and procedures for submission of an application for the renewal of registration of medicines. Applicants shall familiarize with the contents of this document and the governing legislations before they submit applications for renewal of registration of medicines. The Authority has powers to request for information not described in this document that is deemed necessary to ensure the quality, safety, efficacy, need and price of the product. The Authority reserves the right to amend any part of this document whenever it deems necessary.

2. ABBREVEATIONS

API	Active Pharmaceutical Ingredient
APR	Annual Product Report
BE	Bio Equivalence
CDT	Comparative Dissolution Test
CEO	Chief Executive Officer
CEP	Certificate of Suitability of the European Pharmacopeia
COA	Certificate of Analysis
CPP	Certificate of Pharmaceutical Product
FPP	Finished Pharmaceutical Product
GMP	Good Manufacturing Practice
LKR	Sri Lankan Rupees
LOA	Letter of Authorization
MAH	Market Authorization Holder
NMRA	National Medicines Regulatory Authority
PI	Package Insert
PIL	Patient Information Leaflet
SmPC	Summary of Product Characteristics

USD	United States Dollars
WHO	World Health Organization
WHO CRP	World Health Organization Collaborative Registration Procedure
WHO PQ	World Health Organization Pre-Qualification

3. HOW TO APPLY

All renewal applications should be submitted before six months of the expiry date of the active registration certificate.

4. FEES

Application should accompany the receipt for the payment of processing fee prescribed in the Registration (fees) Regulations in force and published by the NMRA.

5. COMPILATION OF THE DOCUMENTS FOR RENEWAL APPLICATION

5.1 Comprehensive table of contents

A comprehensive table of contents should be attached to the dossier with the correct page numbers.

5.2 Cover letter

(a) The cover letter should be prepared in the company letterhead of the market authorization holder (MAH)/authorized importer. It should be signed by the Regulatory Affairs Officer of the company.

(b) The cover letter should not contain any evaluable information.

(c) Written declaration from the authorized importer for the following,

- No changes except variations approved by the NMRA from the date registration was granted
- All variations were approved by the NMRA
- Product maintained its quality, safety, and efficacy in the past 5 years
- All information provided in the application is true and accurate

5.3 Letter of Authorization (for imported products)

A letter from the overseas manufacturer addressed to the CEO/NMRA appointing the applicant as the authorized importer for the product under consideration.

Where the company manufactures the product at two or more places, product license holder or/and manufacturer responsible for release of the product to the market should submit the letter of authorization.

The appointed MAH/authorized importer is responsible for correspondence and complete compliance with regulatory requirements pertaining to the product distribution life cycle in the country.

5.4 Agency transfer approval letter or any other approval issued by the NMRA with regard to administrative changes of the company (if applicable).

5.5 Application Form

The application form for grant / renewal of a certificate of registration of a medicine by a local manufacturer /an authorized importer (Schedule I of Regulation 2 (12) of National Medicines (Registration and Licensing of Medicine Regulations, 2019.) should be completed and duly signed by the regulatory affairs officer.

5.6 Price related information as per the Form, “Submission of price details For Dossiers & Import Licenses - New Registration/Renewal (Additional/RR)” - (Appendix I) should be completed and signed by the regulatory affairs officer.

5.7 A) For imported products Manufacturing site approval letter and a copy of the latest import license issued by the NMRA should be submitted.

B) For locally manufactured products the Latest GMP inspection report and a copy of manufacturing license of the product should be submitted.

5.8 Copy of previous registration certificate

5.9 Justification(s) for lack of certain documents and/or deviations from guidelines

5.10 Particulars of any items supplied together with the drug product, such as diluent, syringe and needle etc. (copy of GMP certificate of the manufacturer, COA, Label, stability data)

5.11 WHO prequalification certificate (if applicable)

5.12 Certificate of Pharmaceutical Product (CPP)

CPP issued by a competent authority in the exporting country should be provided in accordance with the format recommended by the WHO

The CPP should be valid at the time of submission, specific to Sri Lanka and be the original.

5.13 Certificate of Suitability of the European Pharmacopeia (CEP) or GMP certificate of the API/s manufacturer/s.

Any variation relevant to API should be submitted according to the GL-007- Guideline on variations for Medicines published by the NMRA.

5.14 Import details according to the form "Submission of import details for Renewal applications" (Appendix II)

5.15 Copy of Appendix 2 –Consent of WHO PQ holder for WHO to share information with NMRA (mandatory for WHO CRP)

5.16 Copy of Appendix 3-Part A –Expression of interest to the NMRA in the assessment and accelerated registration of PQ products (mandatory for WHO CRP)

5.17 For vaccines and blood products,

5.17.1. Lot release certificates issued by NCL for four batches (mandatory for vaccines & Sera)

5.17.2. Summary lot protocols for minimum four batches /Lots (mandatory for vaccines & Sera)

5.17.3. Prior registration check list on vaccine quality and safety (mandatory for vaccines & Sera)

5.17.4.Vaccine temperature stability profile (Additional stability data to support the assignment of VVM type or to support any on-label claim for elevated temperature storages)

5.17.5. Recommended schedule and route of administration

5.17.6. Local post marketing surveillance data

5.18 Quality Documents as indicated below:

5.18.1 A) A copy of COA of API currently in use

B) Original COA of FPP

5.18.2 Summary of the Annual Product Report (APR), along with the COAs, over the last two years.

5.18.3 Summary of product quality review with the objective of verifying the consistency of the quality of the FPP and its manufacturing process. (See guidance for Quality Document for renewal of registration needed in point A)

5.18.4 Tabular summary of any variations notified, accepted, and pending with the NMRA since the grant of Certificate of Registration

5.19 Report of Bio Equivalence (BE) test if needed or Comparative Dissolution Test (CDT)

5.20 Copy of the updated summary of product characteristics (SmPC)

- Recommended format for the content of the SmPC is provided in Appendix III of this Guideline.

5.21 Updated Original PI and original labels, enclosed with photographs of the product as well as the distributed packaging.

5.22 Patient Information Leaflet (PIL) where applicable

5.23 Two samples of the commercial pack (available smallest pack size)

A. Guidance for Quality Document for renewal of registration

- Rejected batches should not be included in the quality review, but must be reported separately together with the reports of failure investigations, as indicated below.
  - Reviews should be conducted with not less than 10 consecutive batches manufactured over the period of the last 12 months or, where 10 batches were not manufactured in the last 12 months, not less than 25 consecutive batches manufactured over the period of the last 36 months, and should include at least:

1) Review of starting and primary packaging materials used in the FPP, especially those from new sources;
2) Tabulated review and statistical analysis of quality control and in-process control results;
3) Review of all batches that failed to meet established specification(s);
4) Review of all critical deviations or non-conformities and related investigations;
5) Review of all changes carried out to the processes or analytical methods;
6) Review of the results of the stability-monitoring program;
7) Review of all quality-related returns, complaints and recalls, including export- only medicinal products;
8) Review of the adequacy of previous corrective actions;
9) List of validated analytical and manufacturing procedures and their re-validation dates;
10) Summary of sterilization validation for components and assembly, where applicable;
11) Summary of recent media-fill validation exercises;
12) Conclusion of the Annual Product Review;
13) Commitment letter that prospective validation will be conducted in the future; and, the Protocol.

Appendix I

SUBMISSION OF PRICE DETAILS

Dossier Number	
Product (Generic Name with Strength & Dosage form)	
Brand Name (if any)	
Manufacturer (Name & country)	
Name of authorized importer	
Pack Size(s)	

❖ Following details should be submitted for the reference of pricing unit.

1) CIF price/ unit dosage form in USD (i.e. Unit dosage form : /tablet/capsule /vial/ampoule/bottle etc.)	
2) Country of origin price/ unit dosage form	
3) Regional Price/ unit dosage form	
4) Previous Price/ unit dosage form (in SLR) - (This price should be mandatory for all applications except the new applications)	
5) Requested MRP/ unit dosage form in SLR	
6) Remarks (if any)	

❖ For 1, 2, 3: Declaration from the Manufacturer should be attached with the application.

❖ For 4, 5; Declaration from the authorized importer should be submitted.

Submitted by,

…… ……

(Signature) (Date)

E-mail: ……..

Appendix II

Submission of Import Details for Renewal Application

Dossier Number	
Generic Name with Strength & Dosage form	
Brand Name	
Manufacturer (Name & Country)	
Authorized importer	
Pack Size(s) & Pack Type(s)	

- **Following details should be submitted**

1) Proof documents to participation of tenders etc.	
2) Total quantity imported in last two years	**Year** / **Invoice no** / **Date of invoice** / **Quantity**
3) Any clarification for non-availability of import details (if applicable)	

I hereby declared that the above details are true and correct

……. ……

(Name and Signature of the Regulatory Affairs Officer) (Date)

E-mail: ……..

Appendix III

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the finished pharmaceutical product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars
    - Therapeutic indications
    - Posology and method of administration
        - Children and adolescents (4 to 17 years of age)
        - General administration recommendations
        - Special dosing considerations in adults
    - Contraindications
    - Special warnings and special precautions for use
    - Interaction with other fpps and other forms of interaction
    - Use in Pregnancy and lactation
    - Undesirable effects [*See example below*.]
    - Overdose
5. Pharmacological properties
    1.1. Pharmacodynamic properties
        - Pharmacotherapeutic group: {group}
        - ATC code
        - Mechanism of action
        - Pharmacodynamic effects
            - Adults
            - Pediatric patients if recommended

    1.2. Pharmacokinetic properties
        - Absorption
        - Distribution
        - Biotransformation
        - Elimination
        - Characteristics in patients

    1.3. Preclinical safety data

    Data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction
6. Pharmaceutical particulars
    - List of excipients
    - Incompatibilities

      In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. “This medicinal product must not be mixed with other medicinal products “
    - Shelf life
    - Special precautions for storage
    - Special precautions for usage / preparation before use . For Example :
        - Products to be reconstituted - Method of preparation, the diluent to be use and shelf-life after preparation
        - Tablets – Division of the tablet –state whether tablet can be divided or not

        - Special equipment for use, administration or implantation
    - Special precautions for disposal and other handling
7. Administrative Data
8. Holder of Certificate of Product Registration
9. Number of Certificate of Product Registration
10. Date of first authorization/re-registration of the authorization
11. Date of revision of the text