Guideline on Product Registration and Approval of Medicines
Guideline on Product Registration and Approval of Medicines is released under the authority of

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It is the property of:
Maldives Food and Drug Authority
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Guideline on Product Registration and Approval of Medicines

1 INTRODUCTION

Medicine Regulation No: R-46/2014, implemented on 20th January 2015 and the amendment of the Medicine Regulation, of Maldives Food and Drug Authority (MFDA). As per Chapter 11 (of the same regulation), the medicine which are manufactured, sold and imported to the Maldives shall be registered at Maldives Food and Drug Authority. To facilitate the product registration process, this guideline is drawn up in accordance to the chapter 3 (clause 3.1 and 3.2) of the medicine regulation 2015.

The registration process, guideline and the Marketing authorization form applies for all international, domestic, public and private sector without any discernment.

The Authority or/ and National Pharmaceutical Board (NPB) adopts the principle of “Risk- based Approach” for product dossier evaluation which determine he product evaluation route. (Full evaluation or abridge evaluation)

The application to register of the medicines can be made by any pharmaceutical manufacturer within or outside the Maldives. However, the applicant should ensure that all of the information given in the application form and supporting documents are true and valid at the time submitting application.

The technical evaluation of the pharmaceutical product is done by the assigned pharmaceutical officers and approved by the NPB.

The NPB approves for registration of medicines manufactured under internationally recognized Pharmacopoeia, while medicines which are manufactured as per in house specification require adequate justification with provision of reference standards for testing.

2 PURPOSE

This guideline has been developed to guide the medicines importers and pharmaceutical companies or the market authorization holder (MAH) certified and authorized by Maldives...
Food and Drug Authority in the preparation and submission for medicine registration in the form of dossier.

3 SCOPE
This guideline primarily addresses the information to be presented in registration applications for pharmaceutical products.

4 RESPONSIBILITY AND ACCOUNTABILITY
1. Pharmaceutical officers of Medicine Registration Section (MRS)
2. Director, Pharmaceuticals (Regulation)
3. Deputy Director General (Medicine Therapeutic Goods Division)
4. Director General (MFDA)
5. National Pharmaceutical Board

5 Guideline content
5.1 Submission of Dossier
Any local party who is registered as medicine importer in MFDA can submit the dossier for the interested brands to import as per the Reference country Categorization for pharmaceutical product registration (MTG/RE-RP/Li 0015)

5.2 Preparation of dossier

5.2.1 All documents have to be prepared in English language according to the “Application for Registration of Pharmaceutical Product” (Annex 1). If the documents are not in English, a valid translation of the document has to be attached.

5.3 General Requirement of the Dossiers
In general, the following documents are required:

5.3.1 Company Profile
The company profile documents should include the detail of the following:

a. Brief history of company with its detailed address including phone and fax number.
b. Brief description of the Organization.
c. Organization chart
d. List of the product category manufactured
e. Name and qualification of the key personnel (Head of Quality assurance – Quality Control, storage and production) where possible with the signatures of the personnel against name.
f. State whether the company is manufacturing under loan license or not. If so, include details.

5.3.1 Complete form for “Application for Registration of Pharmaceutical Product” (Annex 1) and “Statement by the marketing authorization Holder/Local agent” (Annex 1)

5.3.1.1 The product profile should provide the following information on the finished product;
  a. Generic or INN name
  b. Brand name /Product Name
  c. Dosage Form
  d. Strength of the finished product
  e. Reference of the official standards of the finished product (eg: compendia pharmacopeias or manufacturer’s in-house specification).
  f. List of all the ingredients in the dosage form and their amount on a per unit basis, as per the label claim and batch quantities.
  g. Description of the organoleptic characteristics of the product, including shape, size, superficial markings for identification purposes, color, odor, taste, consistency, type of the tablet coating, type of capsule etc.
  h. Physico-chemical properties such as color, shape, particle size, pH, solubility in water and other solvents, existence/ absence of the polymorphs and pseudo-polymorphs, hygroscopic nature, etc. When describing a liquid, state clearly whether it is in the form of a solution (clear), suspension, emulsion, etc.
  i. Commercial presentation of packaging and pack size in terms of quantity/ weight/ volume, dimension etc.
  j. Description of primary packing materials
  k. Number of units, weight, volume and dimensions
1. Number of secondary packs per standard pallet
m. Note: For drug product in plastic container, studies done on the plastic to demonstrate safety to use shall be provided.
n. Route of Administration
o. Therapeutic class
p. Proposed dispensing category
q. Shelf-life
r. Storage condition

5.3.2 Manufacturer of the Product

5.3.2.1 Manufacturer responsible for lot release of the finished dosage form. Provide full details of name, address, phone, fax, e-mail and contact details.

5.3.2.2 Manufacturer responsible for packaging of the finished dosage form, if different from the above. Provide full details of name, address, phone, fax, e-mail and contact details.

5.3.2.3 Manufacturing license by the relevant authority to perform the activity. Manufacturing license should:
a. Bear the name of the full name of the firm (including site name), the date of certification and identity of issuing authority.
b. Be valid and should have remaining validity of at least 06 months during the time of submission OR
c. If the certificate is nearing its expiration, evidence of application or under process letter for renewal of same issued by the licensing authority must be submitted along with the certificate.
d. Contain the list of products applied for registration.
e. Loan license and contract manufacturing status where applicable must be reflected.
f. If manufacturing license is unavailable, the local agent or manufacturer of the product should submit a commitment letter.
5.3.2.4 Proof that the manufacturing site for the product is GMP compliant (Valid WHO type GMP certificate). GMP certificate should:
   a. Bear the name of the firm, the date of certification and identity of issuing authority.
   b. Be valid and should have remaining validity of at least 06 months during the time of submission OR
   c. If the certificate is nearing its expiration, evidence of application or under process letter for renewal of same issued by the licensing authority must be submitted along with the certificate.
   d. If GMP certificate is unavailable, the local agent or manufacturer of the product should submit a commitment letter.

5.3.2.5 The proof of validation of the manufacturing method for each standard batch size.

5.3.2.6 Standard batch size quantities.

5.3.2.7 Brief profile of manufacturer(s), range of products manufactured and marketed in country of origin.

5.3.2.8 Brief description of 1) manufacturing plant lay-out and machinery employed. 2) Manufacturing and packaging process of the product.

5.3.2.9 List of personnel, their responsibilities and qualifications.

5.3.2.10 Letter from the manufacturer for registering the product (Manufacturer to the Drug Regulatory Authority)

5.3.2.11 Any regulatory decisions taken on this product from any drug regulatory authorities (including recalls, bans alerts etc.)

5.3.3 Technical documents for raw materials

5.3.3.1 A complete technical/quality specifications and methods of analysis of all raw materials must be submitted. These shall include all requirements and test methods applied as a routine to every batch. The description of the test methods shall be detailed enough to enable the test to be carried out in an independent laboratory.
5.3.3.2 The technical/quality specifications of each raw material must be presented in separate lists comprising of all applied tests with the corresponding requirements or test limits. These specifications shall be dated and signed by a person in charge.

5.3.3.3 For substances which are subject of an official pharmacopoeia, the current edition of the pharmacopoeia in which the substance(s) is official should be used. United States Pharmacopoeia (USP), British Pharmacopoeia (BP), European Pharmacopoeia (EP), and other official pharmacopoeia as recognized by the authority should be used. If the procedure used is different from what is described in an official pharmacopoeia, the technical specification shall not be any less stringent than that of the official pharmacopoeia.

5.3.3.4 The technical information for ingredients not subject of any pharmacopoeia shall be presented as follows:
   a. The name of the substance supplemented by any trade or scientific synonyms
   b. Detailed information on physical and chemical properties with emphasis on solubility, crystalline form, particle size and state of hydration of state of other crystal solvents, polymorphism, hygroscopicity, melting point, boiling point, density, viscosity, pKa, oil/water partition coefficient etc.
   c. Detailed description of methods of identification as used for production of the substance, and in the form of tests which ought to be carried out as a routine matter;
   d. Description of purity tests in relation to the sum total of predictable impurities, especially those which may have a harmful effect and if necessary; those which, having regard to the combination of substances to which the application refers, might adversely affect the stability of the medicinal product or distort analytical results.

5.3.3.5 Certificate of Analysis (CoA) of raw materials

   Validated and certified copies of the Certificate of Analysis from the supplier of the raw material(s) or the manufacturer of the finished product should be included in the dossier. The certificate(s) should:

   a. Be on a letterhead or other paper that adequately identifies the company manufacturing the raw material(s) or company using the raw material(s)
b. Name of the material to which it refers

c. Date of analysis and signature by an authorized person over his/her name

d. State the pharmacopoeia specifications and methods against which and by which the tests are performed.

e. All tests and analysis that involve measurement should be reported as the actual numerical results and not description like “complies” or “pass”.

5.3.4 Manufacturing process

Following information with regard to manufacturing process should be submitted:

a. A flow diagram giving the steps of the process and showing where materials enter the process. The critical steps and points at which process controls, intermediate tests or final product controls are conducted should be identified.

b. A narrative description of the manufacturing process, including packaging that represents the sequence of steps undertaken and the scale of production. Novel processes or technologies and packaging operations that directly affect product quality should be described with a greater detail.

c. List of equipment’s used in the manufacture.

d. Appropriate process parameters should be identified, such as time, temperature, or pH in each critical steps of the process.

e. A batch manufacturing formula that includes a list of all components of the dosage form to be used in the manufacturing process, with amounts on a per batch basis and total batch size, including overages, functions and a reference to their quality standards.

f. Detailed aseptic requirements for production of sterile products. This shall include data on how sterilization is carried out and controlled. For aseptically prepared drugs, data must be provided on the microbiological quantity or raw material specification and the property of the filter aid.

5.3.5 Analytical method for finished product

Analytical method for finished product should include the following:

a. Technical/quality specification of the finished product.
b. Identification tests and assay method for the quantification of the active ingredients in the finished product including how the data obtained are to be analyzed.

c. Identification and assay of the active ingredient(s) carried out either in a representative sample from the production batch or in a number of dosage-units analyzed individually. Certain tests procedures for general characteristics of a product shall always be included among the tests on the finished product. These tests should, wherever applicable, relate to the control of average masses and maximum deviations, to mechanical, physical or microbiological tests, organoleptic characteristics, physical characteristics such as density, pH, refractive index, etc. For each of these characteristics, standards and tolerance limits should be specified.

d. Identification tests and assay of preservatives and antioxidants.

e. Validation information, including experimental data for accuracy, specificity, precision, linearity and reproducibility of the analytical procedures used for testing the finished product.

5.3.6 Certificate of Analysis (CoA) of finished product

The CoA of the Finished Product should include the results of all the requirements and test methods stated in the technical/quality specification of the finished product. The Certificate, validated and certified should:

a. Be on a letterhead or other copy that adequately identifies the manufacturer of the product.

b. Be dated with the date of analyses and signed by an authorized person against the name.

c. State the specifications and methods against which and by which the tests are performed.

d. Give all tests and analyses that involve measurement as the actual numerical results and not descriptions like "complies" or "pass".

e. Declare acceptable in case of such document being computer generated.

5.3.7 Disintegration and dissolution profile

Detailed procedures and methods for determining the disintegration and dissolution characteristics of the finished oral solid dosage forms should include:
a. The exact types of equipment, reagents, chemicals etc. used for the test and their reference to compendia pharmacopoeia.

b. The test data listed as numerical values along with the tolerance limits.

c. The raw data for those drugs included in the pharmacopoeia and calculations for those not included.

5.4 Regulatory situation

5.4.1 Evidence supporting the registration status of the product in the manufacturing country and whether or not used in the country (should have the validity of 06 months at the time of submission).

5.4.2 Evidence supporting that product is registered for export (should have the validity of 06 months at the time of submission).

5.4.2.1 CoPP should:

a. Include the date of issue, the name of the product, name of the site and the name of the issuing authority.

b. Be valid and should have remaining validity of at least 06 months during the time of submission OR

c. If the certificate is nearing its expiration, evidence of application or under process letter for renewal of same issued by the licensing authority must be submitted along with the certificate.

d. Originate from the country where the product is being manufactured.
5.4.2.2 If CoPP is unavailable, the local agent or manufacturer of the product should submit a commitment letter.

5.4.2.3 The CoPP should be in the format of the WHO Certification Scheme on the Quality of Pharmaceutical Products.

5.4.2.4 List of countries where the product is registered and currently marketed.

5.4.2.5 Proof of registration of any drug regulatory authority as per the criteria defined in “Reference Country Categorization for Pharmaceutical Registration”.

5.4.2.6 Free sale certificate of the product
   a. If the CoPP format is not as per the format of WHO Certification Scheme on the Quality of Pharmaceutical Products; the document indicating the free sale of the product in the country of origin must be furnished. It must be issued by the authorized authority from the country of origin. It should contain the following:
      ▪ Brand Name
      ▪ Generic Name or INN name
      ▪ Dosage form and strength
      ▪ Complete name and address of the manufacturer

5.4.3 Finish product specification

5.4.3.1 Specify the finish product specification with reference to pharmacopoeia indicating the edition

5.4.3.2 Copy of the finish product specification

5.4.3.3 Limit in % for the assay in active ingredients(s)

5.4.3.4 Additional specifications if any (eg: dissolution etc...)

5.4.3.5 Copy of the Model certificate of analysis for batch release/Certificate of analysis of finished product.

5.4.4 Stability
5.4.4.1 The stability test report should include the following:

a. Report for both accelerated stability study (Temperature 30 ± 2°C and Relative humidity 65 ± 5%) and real time stability study (Temperature 30 ± 2°C and Relative humidity 65 ± 5%).

b. Stability study should be continued for the full period to validate the predicted shelf-life. Where not available, at least 12 months should be completed in case of ongoing real time stability study and letter of commitment for submission of report after the completion of the study should be submitted.

c. The types of studies conducted, protocol used, and the summary of the results of the studies. The summary should include results as well as conclusions with respect to storage conditions and retest date or shelf-life, as appropriate.

d. Result of the stability studies presented in an appropriate format such as tabular, graphical, or narrative.

e. Information on analytical procedures used and validation of these procedures.

5.4.4.2 Information on the stability program inclusive of the following details:

a. Number of batches (minimum of 03 different batches) with the batch number.
b. Product composition.

c. Container/ closure system

d. Storage conditions

e. Parameters studied (e.g. content of active ingredient(s), degradation products(s), pH, appearance, homogeneity of cream, ointment, clarity, dissolution.

f. Testing intervals.

g. Initial values.

5.4.5 Therapeutic Equivalence

5.4.5.1 Demonstrated with evidence in either of the following way:

a. By in vivo bioequivalence studies with a reference product

b. By in vitro dissolution tests with a reference product

5.4.5.2 Bioequivalence (BE) Study reports

▪ Bioavailability studies are necessary to determine the rate and extent to which the active drug ingredient reaches the target site(s) of action after absorption from a drug formulation.

▪ Bioequivalence utilizes the concept of bioavailability in assessing the comparability of finish products containing the same amount of active ingredients but produce by different manufacturers.

5.4.5.3 Oral immediate release pharmaceutical products with systemic action when one or more of the following criteria apply:

a. Critical use medicines

b. Narrow Therapeutic Range (efficacy/ safety margins)

c. Active pharmaceutical ingredient with bioavailability problems or bioequivalence including polymorphs of API, the excipients or the pharmaceutical products designed to act by systemic absorption.

d. Modified release pharmaceutical products designed to act by systemic absorption.
5.4.5.4 Following categories of medicine if presented as tablets or capsules, either as a single ingredient or in combination will require Bio-equivalence studies:
   a. Antibiotics
   b. Antiviral Drugs
   c. Anti-leprosy Drugs
   d. Anti-tuberculosis Drugs
   e. Antimalarial Drugs
   f. Antifungal Drugs
   g. Antiprotozoal Drugs
   h. Antineoplastic Drugs
   i. Immunosuppressive Drugs
   j. Anti-angina Drugs
   k. Anti-arrhythmic Drugs
   l. Anti-hypertensive Drugs and Diuretics
   m. Drug used in heart failure
   n. Steroids
   o. Anti-diabetic Agents
   p. Anti-psychotic Drugs

5.4.5.5 The list of categories for which bioequivalence studies is required is subject to change as deemed necessary by the authority. In such case, the list will be notified through official website of the authority.

5.4.5.6 Comparative Dissolution Study Report
   a. Comparative dissolution study can be used as a substitute for in-vivo pharmacokinetic bioequivalence studies compatible with justification for biowaiver provided.
   b. Biopharmaceutics Classification System (BCS) should be used as the main tool for qualification of biowaiver on the basis of dissolution profiles properties of active pharmaceutical ingredient.
c. Biowaiver based on dose proportionality will be considered for approval of different strengths of a generic product on the basis of dissolution profiles, if the formulations have proportionally similar compositions.

d. Approval of generic formulations using comparative in vitro dissolution studies should be based on generation of comparative dissolution profiles rather than a single point dissolution test.

e. The dissolution profile of the generic and test products should be made under the same test conditions using an apparatus that conforms to the USP and BP specifications using either the paddle method at 75 rpm or the basket method at 100 rpm in pH 1.2, 4.5 and 6.8 buffers at 37°C. Similarity factor should be used to compare dissolution profiles.

5.4.6 Specimen of Package, Label and insert information

5.4.6.1 Specimen of the original package including package, label and insert must be furnished. This specimen must be same as commercially available specimens.

5.4.6.2 At least three specimens must be included in the dossier.

5.4.6.3 The product label should contain the following information where it is possible;

5.4.6.3.1 If manufactured and registered in category 1 of Reference country categorization for pharmaceutical product registration
   a. Product Name
   b. Dosage Form
   c. Name and strength of the active ingredient(s)/content of formulation with quantity of ingredients per dosage unit.
   d. Batch number
   e. Manufactured Date
   f. Expiration Date
   g. Pharmacopeia Standard
   h. Route of administration
   i. Storage conditions in detail (Eg: Do not store above 30 c, protect from light etc...)
   j. Name and address of the manufacturing site, marketing authorization holder (MAH) or registration code (RC) number specified by the relevant Authority
k. If only MAH or RC number is mentioned in outer pack, the manufacture plus MAH or Manufacturer plus RC number will be added to ADL

l. Net content of the package

m. Pack sizes (unit/volume)

n. Warning/cautions

o. Precautionary information (eg: Keep the medicine out of reach of children).

p. Direction for handling and storage

q. Label Language in English/Dhivehi (Attach a copy)

r. Copy of the packing insert

s. Samples of the packing with labels (3 nos)

5.3.6.3.2 If manufactured and registered in other than category 1 of Reference country categorization for pharmaceutical product registration:

Specimen of Package, Label and insert information, which includes:

a. Product Name

b. Dosage Form

c. Name and strength of the active ingredient(s)/content of formulation with quantity of ingredients per dosage unit.

d. Batch number

e. Manufactured Date

f. Expiration Date

g. Pharmacopeia Standard

h. Route of administration

i. Storage conditions in detail (Eg: Do not store above 30 c, protect from light etc...)

j. Name and address of the manufacturing site

k. Net content of the package

l. Pack sizes (unit/volume)

m. Warning/cautions

n. Precautionary information (eg: Keep the medicine out of reach of children).
o. Direction for handling and storage
p. Label Language in English/Dhivehi (Attach a copy)
q. Copy of the packing insert
r. Samples of the packing with labels (3 nos)

5.4.7 Product samples:

5.4.7.1 Samples of finished product submitted for registration shall be taken at random from an actual product batch.

5.4.7.2 Samples submitted must be intact, it must be in final commercial pack with original labels, and package inserts.

5.4.7.2.1 For the products with various ingredients (such as vitamins) may not have all the ingredient mentioned in the outer pack. For such cases label must be fixed as per the recommendation of MFDA.

5.4.7.3 Product sample size may vary depending on the type of packaging used:
   a. Minimum of 01 multi dose container, if packed in multi dose container and if packed in strips/blisters; minimum of 02 boxes but not less than following sample size
   b. Tablets, Capsules, suppositories (60 nos).
   c. Oral liquid, Small Volume Parenteral including solution and powder for injection, IV fluids (Large Volume Parenteral), Eye/Ear Drops, cream/ointment/location, Transdermal patch/Oral powder/ inhalation and nasal preparation, etc. - at least 03 nos and must be intact in its primary packaging.

5.4.7.4 Product samples submitted must have a remaining shelf-life of at least half of its shelf-life.

5.4.7.5 If the product is without an out carton, the inner label should bare all the information that is required.

5.4.7.6 The color of the labels should be differentiated between strengths of products. The label must be made from good quality material.
5.4.8 Price Structure

5.4.8.1 The price structure should:
   a. Indicate price applicable to the wholesaler, retailer and the maximum retail price.
   b. Indicate value either in Maldives market in USD

5.4.9 Documents required for medicines manufactured and registered in Category 1 country

   a. Good Manufacturing Practice (GMP) of the manufacturing site of the product

   b. Certificate of pharmaceutical product (COPP) certificate from the regulatory authority in the manufacturing country

   c. Stability tested reports of the product

   d. Finished product specification

   e. Second country registration certificate is not required for this category.

   f. Products registered under this category will be valid for a period of 5 years.

5.4.10 Multinational companies where the parent company is from category 1 countries, second country registration in category 1 is not required. However, supporting documents from the parent company is required.

   a. A document from the parent company stating the product manufactured from the proposed site is up to the standard of the parent company OR, a recent audit or assessment report of the site by the parent company etc

   b. Products registered under this category will be valid for a period of 5 years.

5.4.11 Documents required for medicines manufactured and registered in Category 2 country

   a. Products manufactured from countries in category 2 and regulated by the respective authorities in the country of manufacture, shall submit: Full dossier of the product as per this Guideline
5.4.12 If product is registered by submitting Second country registration certificate in category 1 validity of the registration is for a period of 3 years.

5.4.13 OR MFDA to conduct GMP inspection of the manufacturing facility (Products registered under this criteria will be valid for a period of 2 years)

5.4.14 OR to submit analysis report of 3 batches of the product tested form a WHO collaborating center/OR to submit batch certificates for individual batches imported during import.(Products registered under these criteria will be valid for a period of 3 years)
5.5 **Arrangement of the document**

5.5.1 All the documents should be arranged according to the “Application for Registration of Pharmaceutical Product”.

5.5.2 All regulatory certificates must be notarised.

5.5.3 All the certificates should have a validity period of not less than 6 months at the time of submission. If validity period is less than six months at the time of submissions a commitment letter is required. However, registration certificate will be provided upon receiving of the renewed document.

5.5.4 If the expiry dates are not mentioned in the certificates, there should be an explanatory note or an official document stating the reason.

5.5.5 Documents must be submitted on working from 08:00 to 14:00 hours. You may call +960-3014316, +960-33014308, Medicines and Therapeutic Goods Division, Maldives Food and Drug Authority for further clarification.

5.5.6 Incomplete documents and/or documents that do not comply with the above-stated notes will not be received.

5.6 **Processing of Application**

5.6.1 Once received the dossier from the Dhirithi Portal documents will be checked and verified within 15 (fifteen) working days.

5.6.2 Evaluation will be completed within 60 (sixty) working days. This date will be considered from the third day of the payment of submission fees.

5.6.3 Brief description of product evaluation summary will be submitted to the National Pharmaceutical Board for the final decision.

5.7 **Acceptance of application**

5.7.1 If all the documents are there and acceptable, it will be notified from Dhirithi Portal.
5.8 Rejection of the application

5.8.1 In any circumstances if the dossier is rejected, the submitted samples will be non-refundable.

5.8.2 The submitted samples will be discarded after 3 months from the date of rejection.

5.8.3 An application for registration will be rejected in following if:
   a. The applicant fails to submit all the required documents and complete the registration formalities.
   b. Once the application is rejected, the applicant will be notified via dhirithi portal

5.8.4 The dossier submission fee is MVR 100 per product (Even if it is same product with different flavors, different volumes and different pack size). The process after the acceptance of dossier will only be continued once this amount has been paid and the budget slip is submitted to MTG.

5.8.5 If the product is successfully approved for registration, a fee of MVR 300 will be charged.

5.8.6 The fees has to be paid before 12PM on all the working via bandeyri pay (https://bandeyripay.finance.gov.mv/)

5.8.7 Once fees are requested it has to be notified to the MTG of MFDA.

5.8.8 In any circumstances if the dossier is rejected, the submission fee is not refundable.
5.9 Evaluation of the dossier

5.9.1 The pharmaceutical officers of the Regulation Unit of Medicine and Therapeutic Goods Division do the technical evaluation of the medicinal product dossier.

5.9.2 Once the dossier is accepted and the submission fees are paid the evaluation process will be started and completed within 60 (sixty) working days.

5.9.3 Once the evaluation is completed, the “Product Evaluation Summary” (MTG/RE-ES/Re 0005) will be submitted to the national Pharmaceutical Board.

5.9.4 The National Pharmaceutical Board will make the final decision for the product.
5.10 Regulatory Decision
The National Pharmaceutical Board makes a regulatory decision based on the outcome of the evaluation of the dossier. The decision will be accordingly communicated to the applicant. A decision will be made by National Pharmaceutical Board within 20 (twenty) days after the evaluation has been completed.

5.11 Approval of Product
a. If the product is approved from the National Pharmaceutical Board, it will be notified to the Local agent via dhirithi portal 5 working days.
b. The budget slip (registration fees) will be issued.
c. Once the registration fees are paid the certificate will be issued

5.12 Rejection of a Product

5.13 If the product is rejected from the National Pharmaceutical Board, it will be informed to the Local agent via dhirithi portal within working 5 days

Multiple Applications

5.13.1 A separate application is required for each product i.e. products containing the same ingredients but made to different specifications (in terms of strength/content of ingredient(s), dosage form, description, pack size etc.) or by a different manufacturer shall require separate applications for product registration.

5.14 Issuing Product Registration Certificate (CoPP)
a. The certificate for registered product will be issued in the specified format.
b. The registration certificate shall be issued within 10 (ten) working days from the date of registration fees are paid, unless otherwise a longer period is required, in which case, the party will be informed.

5.15 Rejection, Cancellation, Suspension of Registration, temporary and permanent ban of the product and/or manufacturer
a. The Maldives Food and Drug Authority may reject, cancel or suspend the registration of any product if there are deficiencies in safety, quality or efficacy of the product or failure to comply with conditions of registration.
b. A company or manufacturer can be banned temporarily or permanently if repeated incidents of quality failure are identified from their products. If the company is permanently banned, the particular company will not be allowed to enter the Maldives
market until a period of minimum 05 (five) years. After 05 (five) years from the date of banned, they can apply for the registration with the registration certificate of any regulatory Authority in category 1 of Reference country categorization for pharmaceutical product registration and the decision will be made from the National Pharmaceutical Board.

c. If a company /manufacturer is temporarily banned, the products of that company can only enter back to the market as a new applicant under the current procedure. All products of that company must be registered as per the criteria established by the MFDA

5.15.1 Cancellation of Registration

- The Authority may, in the interest of public safety, reject or cancel the registration of any product, if:
  a. Any of the conditions of registration of the product has been contravened.
  b. Any report on adverse drug reactions of serious nature has been received from national or international sources;
  c. 
  d. MAH defaults timely renewal beyond three month of grace period;
  e. For any other matters as specified by the Board at the time of cancellation.

5.15.2 Renewal of Product Registration

5.15.2.1 Application for renewal shall be submitted for re-registration at least 60 days before expiry date of registration along with the processing fee.

5.15.2.2 The procedure for the renewal of the registration is same as the initial registration. However, one-time renewal of registration shall be granted with the fulfillment of the following conditions and documents.

5.15.2.3 Following mandatory conditions must be fulfilled by the product in question for renewal with minimal documents:
  a. There should not be change in the manufacturing site/premise of the particular product

5.15.2.4 Documents required for re-registration:
  a. Product Name
b. CoPP

c. GMP Certificate

d. Manufacturer Name

e. Stability

f. Price (if any changes were made)

g. Samples of the packing with labels (3 nos)

5.15.2.5 There should not be change in the ingredients used for the formulation of the particular product;

5.15.2.6 There should not be change in the formulation including color, size, and dosage

5.15.2.7 Documents required for registration of Pre-Qualified Products

a. Proof of pre-qualification approval if the medicine is prequalified;

b. The above evidence either must be provided in original copy or notarized copy, if original copy is not available.

c. CoPP

d. GMP Certificate

e. Manufacturing license

f. Price (if any changes were made)

g. Samples of the packing with labels (3 nos)

5.16 Approved Drug List

5.16.1 Approved Drug List (ADL) (MTG/RE-AL/Li 0009) is the approved list of medicines which can be imported and sold within the country. This list is updated on the 10th of every month and uploaded to the Ministry of Health’s website (www.health.gov.mv).

5.16.2 This list has 5 categories which are:

a. OTC: Drugs which can be sold over the counter without prescription.

b. POM: Drugs which can be sold in the pharmacy with prescription only.

c. Restricted for Hospital use only: Drugs should be sold only in hospitals not in pharmacies.

d. National programmed drugs: only the department who is conducting national awareness programs regarding the drugs should sell Drugs.
5.16.3 Once the product is approved from the National Pharmaceutical Board, it will be added to the next ADL.

5.16.4 Addition to ADL

5.16.4.1 Once the product is approved from the National Pharmaceutical Board, the form for “Approval for Addition of Pharmaceuticals to Approved Drug List” (MTG/RE-AA/Fo 0010) will be filled and approved by the Division Head and authorized by the Head of MFDA, prior to the addition of the product to the ADL.

5.16.5 Deletion to ADL

5.16.5.1 For any reason if any products are to be deleted from ADL, the form for “Approval for Deletion of Pharmaceuticals from Approved Drug List” (MTG/RE-DA/Fo 0011) will be filled and approved by the Division Head and authorized by the Head of MFDA, prior to the deletion of the product to the ADL.

5.16.6 Modification to ADL

5.16.6.1 For any reason if any products are to be modified from ADL, the form for “Approval for Modification / Changes / Amendments to Approved Drug List” (MTG/RE-MA/Fo 0012) will be filled and approved by the Division Head and authorized by the Head of MFDA, prior to the deletion of the product to the ADL.

5.17 Product Registration Transfer

5.17.1 The market authorization of the registered product may be transferred to another individual or firm authorized by the MFDA. However, following conditions and data requirements for product registration transfer must be fulfilled.

5.17.2 Conditions for transfer:

5.17.2.1 An application to transfer the marketing authorization of a product shall be submitted by the proposed new MAH.

5.17.2.2 The manufacturer agrees to withdraw the authorization granted previously to the existing MAH and issue new letter of authorization to the proposed new MAH.
5.17.2.3 The existing product registration shall have a remaining validity period of at least one year. If the period is less than one month, the product must be renewed by the existing MAH before the transfer application is submitted.
5.18 Responsibility of Marketing Authorization Holder

5.18.1 Ensure the medicine(s) are available in the market at all times without interruption or shortages.

5.18.2 Ensure the medicine(s) shall be sold (both wholesale and retail) at the price as mentioned in the Dossier.

5.18.3 Take responsibility to maintain the traceability and recall of the product from all wholesalers and medicine outlets in case of issues safety, quality and/or alert on the product.

5.18.4 Provide periodic safety updates issued from the manufacturer of the medicine(s) annually to MFDA.

5.18.5 Provide and facilitate public awareness on the medicine(s) as per the recommendations and approvals from MFDA.

5.18.6 Liaise with the manufacturer and provide product updates and changes if any.

5.18.7 Provide information on any changes to the product formulation including label and information submitted for registration.

5.18.8 Comply with existing Laws, Regulations and Rules.

5.19 Clinician’s Request for Approval of New Medicine

5.19.1 This form is introduced to the doctors to request to add new chemicals, new dosage form or new strengths, to the Approved Drug List upon the requirement of the patients, and to make sure to maintain the uninterrupted availability of the medicines.

5.19.2 Required Documents

5.19.2.1 A completely filled “Clinician’s Request for Approval of New Medicine” signed by the requesting doctor and approved by head of the applicants’ organization/Health facility.

5.19.2.2 Additional information and the picture shots of the product
5.19.3 **Acceptance of Form**

5.19.3.1 If the application is for a new chemical, new strength and new dosage form, and the form is filled completely, the application will be accepted.

5.19.3.2 Once the form is accepted, the application will be sent to MFDA’s main entry.

5.19.3.3 Once received from the main entry, the product will be entered to the “Clinician’s Request Evaluation Data Sheet” (MTG/RE-PE/Re 0026)

5.19.3.4 Evaluation will be carried out within the next 45 (Forty-five) working days.

5.19.3.5 Once the product has been approved, the process in 5.13.4 will be carried out.

5.19.4 **Rejection of form**

5.19.4.1 If the application is incomplete or if the application is form for an existing medicine in the ADL, the application will be rejected and informed to the applicant during working 07 days.

5.19.4.2 Evaluation of the submitted product will be completed in 45 days after expectance and product will be approved once the final decision has been taken by the National Pharmaceutical Board.

5.20 **Special approvals given for hospitals to import and use hospital use medicines in their facilities.**

5.20.1.1 In case of importing hospital use medicines which is required in low volume/quantity, and for which there is difficulties in getting the required documentation, exemption approvals will be given to hospitals to import and use these medicine in the hospital settings only, as these medicines are required for critical care in hospitals. The approvals will be given under a set of conditions by means of a signed agreement between MFDA and the importing hospital.

6 **Legal basis and references**


   b. Medicine regulation amendment R-49 (2016)

   c. Health service act (29/2015)
7 Records

a. Reference county categorization for pharmaceutical product registration (MTG/RE-RP/Li 0015)

b. Application for Registration of Pharmaceutical product (MTG/RE-MF/Fo 0001)

c. Dossier acceptance form (MTG/RE-AF/Fo 0009),

d. Budget slips (MTG/RE-BS/Re 0030).

e. Dossier rejection form (MTG/RE-AF/Fo 0008)

f. Product Registration Summary Sheet (MTG/RE-AS/Re 0001).

g. Product Evaluation Summary (MTG/RE-ES/Re 0005)

h. Approved Drug List (ADL) (MTG/RE-AL/Li 0009)

i. Approval for Addition of Pharmaceuticals to Approved Drug List (MTG/RE-AA/Fo 0010)

j. Approval for Deletion of Pharmaceuticals from Approved Drug List (MTG/RE-DA/Fo 0011)

k. Approval for Modification / Changes / Amendments to Approved Drug List (MTG/RE-MA/Fo 0012)

l. Clinician’s Request Evaluation Data Sheet (MTG/RE-PE/Re 0026)
8 Annexes

a. Application for Registration of Pharmaceutical Product (Annex 1)
b. Statement by the marketing authorization Holder/Local agent (Annex 1)
c. Clinician’s Request for Approval of New Medicine (Annex 2)
ANNEX 1: Application for Registration of Pharmaceutical Product

<table>
<thead>
<tr>
<th>Serial #</th>
<th>REQUIREMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Applicant information:</td>
<td></td>
</tr>
<tr>
<td>1) A letter of appointment from applicant/local agent bearing all the responsibilities of the manufacturer in regard to the product. (As per the format given in ANNEX 1)</td>
<td></td>
</tr>
<tr>
<td>B. Pharmaceutical Product Information sheet:</td>
<td></td>
</tr>
<tr>
<td>The following information shall be provided:</td>
<td></td>
</tr>
<tr>
<td>1) Product name/Brand Name of the product</td>
<td></td>
</tr>
<tr>
<td>2) Generic name of the product</td>
<td></td>
</tr>
<tr>
<td>3) Active pharmaceutical ingredient[s](use INN if any)</td>
<td></td>
</tr>
<tr>
<td>4) Non-active ingredients</td>
<td></td>
</tr>
<tr>
<td>5) Strength per unit dosage unit</td>
<td></td>
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<tr>
<td>6) Dosage form</td>
<td></td>
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<tr>
<td>7) Pack size:</td>
<td></td>
</tr>
<tr>
<td>7.1 Description of primary packing materials</td>
<td></td>
</tr>
<tr>
<td>7.2 Weight, volume and Dimension</td>
<td></td>
</tr>
<tr>
<td>7.3 Description of secondary packaging material</td>
<td></td>
</tr>
<tr>
<td>7.4 Number of units, weight, volume and dimensions</td>
<td></td>
</tr>
<tr>
<td>7.5 Number of secondary packs per standard pallet</td>
<td></td>
</tr>
<tr>
<td>Note: For drug product in plastic container, studies done on the plastic to demonstrate safety to use shall be provided.</td>
<td></td>
</tr>
<tr>
<td>8) Route of administration</td>
<td></td>
</tr>
<tr>
<td>9) Therapeutic class</td>
<td></td>
</tr>
<tr>
<td>10) Proposed dispensing category</td>
<td></td>
</tr>
<tr>
<td>11) Shelf life</td>
<td></td>
</tr>
<tr>
<td>12) Storage condition</td>
<td></td>
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</tbody>
</table>

C. Manufacturer of the product:

<table>
<thead>
<tr>
<th>Medicine and Therapeutic Goods Division, Maldives Food and Drug Authority</th>
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<tbody>
<tr>
<td>Rec. No: MTG/RE-MF/Fo 0001</td>
<td>Rec. Name: Application for Registration of Pharmaceutical Product</td>
</tr>
<tr>
<td>Issue No: 01</td>
<td>Issue Date: 02.07.2018</td>
</tr>
<tr>
<td>Prepared by: Director, Pharmaceuticals</td>
<td>Approved by: Deputy Director General, Pharmaceuticals</td>
</tr>
<tr>
<td>Revised Date: 21.02.2019</td>
<td>Copy Letter: MTG/RE-GLN 002</td>
</tr>
<tr>
<td>Verified by: Technical Committee of MTG</td>
<td>Page No: Page 1 of 6</td>
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</table>
1) Company profile (for new companies and re-registration or changes for existing companies)

2) Manufacturer responsible for lot release of the finished dosage form. Provide full details of name, address, phone, fax, e-mail and contact details.

3) Manufacturer responsible for packaging of the finished dosage form, if different from the above. Provide full details of name, address, phone, fax, e-mail and contact details

4) Manufacturing license by the relevant Authority to perform the activities in (2) & (3)

5) Proof that the product is a WHO pre-qualified product if applicable

6) 6.1 Proof that the manufacturing site for the product is GMP compliant (Valid WHO type GMP certificate) (should have the validity of 06 months at the time of submission)

6.2 The agency approving the GMP of the site (WHO Compliant GMP Certificate)

7) The proof of validation of the manufacturing method for each standard batch size

8) Standard batch size quantities

9) Technical specifications of all raw material(s) and source (s), including steps taken to assure consistent quality of starting materials.

10) Brief profile of manufacturer(s), range of products manufactured and marketed in country of origin.

11) Brief description of 1) manufacturing plant lay-out and machinery employed. 2) Manufacturing and packaging process of the product.

12) List of personnel, their responsibilities and qualifications

13) Letter from the manufacturer for registering the product (Manufacturer to the Drug Regulatory Authority)

14) Any regulatory decisions taken on this product from any drug regulatory authorities (including recalls, bans alerts etc)

D. Regulatory situation:

1) Evidence supporting the registration status of the product in the manufacturing country and whether or not used in the country

2) Evidence supporting that product is registered for export.

3) Valid Certificate of Pharmaceutical Product (CPP), in accordance to the WHO Certification Scheme (should have the validity of 06 months at the time of submission)

4) List of countries where the product is registered and currently marketed.

5) Documentation supporting registration/licensing status of the product in countries other than country of origin. (refer to “reference county categorization for pharmaceutical product registration” MFDA/MTG-RPR/LS-13)

6) Free sale certificate of the product

E. Finish product specification:

1) Specify the finish product specification with reference to pharmacopoeia indicating the edition

2) Copy of the finish product specification

3) Limit in % for the assay in active ingredients(s)

4) Additional specifications if any (eg dissolution etc)

5) Notarized of the Model certificate of analysis for batch release/Certificate of analysis of finished product

F. Stability

1) Provide the stability testing data for the product
2) Specify the conditions for:
   2.1 Satisfactory accelerated testing
      2.1.1 Type of container
      2.1.2 Conditions (temperature/relative humidity/Duration)
      2.1.3 Number of Batches
      2.1.4 Batch size
      2.1.5 Date of study

   2.2 Satisfactory real time testing
      2.2.1 Type of container
      2.2.2 Conditions (temperature/relative humidity/Duration)
      2.2.3 Number of Batches
      2.2.4 Batch size
      2.2.5 Date of study

3) Is the stability testing done on the product of the same formula, manufactured on the same site and packed in the same packing material as the product that will be supplied?

G. Therapeutic Equivalence

1) Demonstrated with evidence in either of the following way:
   1.1 By In vivo bioequivalence studies with a reference product

   1.2 By in vitro dissolution tests with a reference product

H. Sample, Label and insert information

   1) Shelf life

   2) Storage conditions in detail (Eg. Do not store above 30°C, protect from light etc)

   3) Label Language (Attach a copy)

   4) Copy of the packaging insert

   5) Samples of the packing with labels (3 nos)

   6) Free non returnable Product samples:
      6.1 Tablets/capsules 60 nos
      6.2 syrups : 3 nos
      6.3 Injectablez : 3 nos

I. Price

   1) Cost price in USD

   2) Proposing price for retailing it in Maldives market in USD
Special Notes:

1. On Documents:
   (a) Arrange the documents according to the checklist
   (b) Table of contents and page number should indicate the location of documents inside the dossier
   (c) Use identifying markers/separators in between sections
   (d) All regulatory certificates must be notarised
   (e) Incomplete documents and/or documents that do not comply with the above-stated notes will not be received.
   (f) Documents must be submitted after setting up appointment. You may call +960-3014316, +960-33014317, Medicines and Therapeutic Goods Division, Maldives Food and Drug Authority to set up appointment
   (g) The dossier submission fee is MRF 100 and if the product is successfully considered for registration a fee of MRF 300 is charged. The fee has to be paid to the finance section of the Maldives Food and Drug Authority after the dossier is received.

2. On Registration process:
   (a) Follow-up on the product application status will be through an official letter
   (b) The final decision on registration of the products is by the Board for Pharmaceuticals
   (c) The Board for Pharmaceuticals and the Maldives Food and Drug Authority registers medicines based on set criteria. All applicants will be informed of the results of the product evaluation process.
   (d) Applicants who wish to know why their product has not passed registration may make a formal inquiry if they so desire so that reasons for disqualification may be informed.
   (e) Applicants must name a designated person for correspondence including telephone and email address
   (f) The address of the MFDA is:

   Medicines and Therapeutic Goods Division
   Maldives Food and Drug Authority
   Phone: +960-3014316, +960-33014322
   Email: mtg@health.gov.mv
Statement by the Applicant (Local)

1) I have received and accepted the entire dossier from ___________________________ (Company name and address) for the product __________________________________________________________________________________ (Name of the product, Brand/ Generic/ Dosage Form/ Strength).

This dossier includes all data in support of the original Marketing Authorization as per the format of MFDA.

2) I hereby agree that I have sole responsibility for the mentioned product including obtaining approvals for any subsequent product variation and maintenance of the product registration.

3) I declare that information submitted in this application is correct and complete. I authorize the Maldives Food and Drug Authority to obtain information from any institution previously or currently associated with my company. If any information supplied by me is considered to be false, incomplete or misleading in any respect, Maldives Food and Drug Authority has the right to take action as it believes necessary including the disclosure of the information to any person or body the Maldives Food and Drug Authority considers has a legitimate interest in receiving it and I consent to such disclosure. I understand the Maldives Food and Drug Authority reserves the right to vary or revoke any decision made on the basis of untrue, incomplete or misleading information. Moreover I will co-operate with any person representing the Maldives Food and Drug Authority, by providing additional information or making the manufacturing premises available for inspection as required.

4) I also acknowledge the responsibility in the event of pharmacovigilance issues or quality defects associated with the product that may occur after the registration.

Signed:
Full Name:
Identity Card Number:
Full Address:
Status of the signatory:
(To be signed by the managing director/president/CEO or an equivalent person who has overall responsibility for the company or organization)
Official company stamp:
Telephone Number:
Fax Number:
E mail contact details:
Date:

(*) The applicant shall be responsible for the product and all information supplied in support of his application for registration of the product.

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<td>Issue No: 02</td>
<td>Issue Date: 13.02.2020</td>
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<td>Revised Date: 18.10.2021</td>
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ANNEX 2: Clinician’s Request for Approval Form

Clinician’s Request for Approval of New Medicine

This form may be completed by a clinician, but it must be signed by the Medical Director of that institute.

1. Brand name: .................................................................

2. Generic name: .................................................................

3. Dosage form: .................................................................

4. Strength: .................................................................

5. Pharmacological classification .................................................................

6. Clinical indication: .................................................................

7. Name of manufacture and country of origin: .................................................................

Proposed category for the medicine (Eq: POM, OTC, Restricted for Hospital and institutional use only(HI)): .................................................................

8. What other similar acting drugs and dosage forms are presently included the list of Approved drugs:

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

9. What are the therapeutic advantages of this drug over similar acting drugs already in the list?

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

9. Which of the similar acting drug (s) in the list should be deleted in favor of this new drug

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

11. Describe the major side - effects reported for this new drug:

.................................................................................................................................
12- What contradictions and precautions have been designated for this new drug?

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

13- Indicate the source of your information about this drug including pertinent publications and references:

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

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

Details of requesting Clinician

Full name & signature

________________________________________

Department Date Maldives Medical & Dental Council Registration Number

________________________  ____________

Clinician Seal

Approved by Medical Director

Full name & signature

________________________

Date

Medical Director’s Seal

Note:

1. Upon approval of the requested medicines by the National Pharmaceutical Board, it will be added to ADL for a period of one year.

2. At the end of one year, if the medicine is not imported, or if the medicine is not registered it will be deleted from ADL.

3. Please note that this form must be complete as evaluation and approval is based on the information provided by the clinicians. Hence, incomplete form will be rejected.

*For official use only*

Check and Received by:

Designation:

Signature:

Date: