

Guidelines for application for Registration of Medicinal Products 2006(DRA)



Contact details: Drug Regulatory Authority, Thimphu Bhutan
Telephone # 00975-2-334271, Fax: 00975-2-335803
Email : dra@health.gov.bt URL : www.health.gov.bt/dra.php

Guidelines for application for Registration of Medicinal Products 2006(DRA)

The guidelines outlined in this document are primarily drawn up in accordance to the legal requirements of **the Medicines Act of the Kingdom of Bhutan 2003** and **Bhutan Medicines Rules & Regulation 2005**.

1.0 DRUG DEFINITION

Defined in the Act, "Medicinal Products" include

- i) All the substances intended for internal or external use of human beings or animals and intended to be used in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals; and
- ii) Such substances intended to affect the functioning of any structure found in the human and animal body
- iii) Any other substances or device declared by the board to be a medicinal product or a medicine or a drug and this may belong either to modern or traditional system of medicine

1.1 PROVISIONS UNDER THE ACT

-All medicinal products, manufactured, sold, and distributed and imported/ exported from Bhutan should be registered under the provisions of the act.

-Drug manufacturers and dealers within or outside Bhutan intending to sell or distribute their products in Bhutan should register their products.

2.0 APPLICATION FOR DRUG REGISTRATION:

- The application for registration will be made along with the required documents in Form I of Bhutan Medicines Rules & Regulation 2005 (Annexed Form I).
- The documents required for registration should be in English or *Dzongkha* and submitted in bond form in A4 size paper.
- The documents for registration should be processed only if they are complete and as per specifications.
- Separate applications should be made in respect of different formulation of same medicinal product. (i.e. products containing the same ingredients but made to different specifications (in terms of strength/content of ingredient(s), dosage form, description, etc.) or by a different manufacturer).

Guidelines for application for Registration of Medicinal Products 2006(DRA)

2.1 Data Requirements

All the certificates/testimonies for registration of medicinal products should be attested by the Public Notary or a Court of Justice in case of duplicate.

Medicinal products excluding *gSo-ba Rig-pa* and traditional medicines require the following documents:

2.11 General Documents

- i) Company profile
- ii) cGMP certificate
- iii) Manufacturing licence
- iv) WHO Model Certificate of Pharmaceutical Product
- v) Free Sale Certificate
- vi) *Summary of product information sheet:* Name and Strength of the Active Ingredient (s), Indication, Recommended Dose , Clinical Use(s) of product, State route of administration, contraindication, Warning and precautions, Interactions with other medicaments, Side effects, Symptoms and Treatment of Overdose, Symptoms of overdose/poisoning, and where possible recommended treatment and antidotes for overdose/poisoning, Storage condition.
- vii) Letter of authorization from the manufacturer for registration (in case of registration by a dealer)
- viii) Dealership certificate (in case of registration by a dealer)
- ix) Credentials of the dealer
- x) Product sample
- xi) Price structure

2.12 Pharmaceutical Documents

- i) Physico-chemical properties of active and inactive ingredients: (*Colour, odour, taste, physical state(powder, amorphous, crystalline, liquid), Solubility, melting point, hygroscopicity, polymorphism, pKa, pH values*)
- ii) Analytical method for identification of active substance and excipients
- iii) Manufacturing process for the product
- iv) List of raw material and specifications
- v) QC procedure and report on raw materials
- vi) Finished product specifications
- vii) Disintegration and dissolution profile.
- viii) Analytical method for the finished product
- ix) Certificate of analysis
- x) Stability test report for Zone IV
- xi) Packaging specifications
- xii) Specimen of package, label and package insert
- xiii) QC procedure and report on label and package

Guidelines for application for Registration of Medicinal Products 2006(DRA)

2.13 Pharmacological Documents:

- i) Data on basic pharmacological and microbiological studies
- ii) Pharmaco-kinetics data. (Absorption, plasma-protein binding, distribution, biotransformation, metabolism, excretion, etc.)
- iii) Bio-availability and bio-equivalence data (in case of generic drugs)
- iv) Data on clinical studies Phase I, Phase II, Phase III & Phase IV *Clinical pharmaco-kinetics *
- v) Toxicity data *
- vi) Teratogenicity data *
- vii) Mutagenicity data *

The pharmacological documents marked with asterisk (*) is applicable only for registration of new molecules or new formulation of old molecules or molecules with very little post-marketing experience.

2.2 Some products are registered with some exceptions considering the national needs.

2.3 Wherein there is a proof of the product being already registered in a developed country, appropriate considerations wherever applicable are granted in the registration of the products.

2.4 Any person who wishes to import any product for the purpose of research in a school of pharmacy or research or training institution or in order to obtain samples for the purpose of registration may be exempted from registration with prior approval from the Authority.

2.5 The applicant (if said company is not the product owner) should be authorized in writing by the product owner to be the holder of the product registration certificate and be responsible for all matters pertaining to the registration of the product.

3.0 RESPONSIBILITY OF MARKETING AUTHORIZATION HOLDER (i.e. THE APPLICANT FOR PRODUCT REGISTRATION)

3.1 The applicant should be responsible for the product and all information supplied in support of his application for registration of the product.

3.2 He should be responsible for updating any information relevant to the product/application. The DRA should be informed in a timely manner any change in product information during the course of evaluation, and after product registration, especially if the information pertains to rejection/withdrawal, additional data on product efficacy and safety or current Good Manufacturing Practice (cGMP) compliance of the manufacturers.

Guidelines for application for Registration of Medicinal Products 2006(DRA)

- 3.3** The marketing authorization holder must assume responsibility for the quality, safety and efficacy of his products.

Letters of authorization and certifications should be valid and current at the time of submission.

4.0 TEMPORARY REGISTRATION OF DRUGS

Temporary registration will be granted upon request by relevant government agencies for medicinal products specially required in emergency, disease out-break and for specific needs of patients.

The application for temporary registration should be made in Form VI of Rules & Regulation 2005 with the following documents (Annexed Form VI):

- Therapeutic indication details
- Free sale certificate of the product
- Product registration certificate issued in the country of origin
- Package specification
- Finished product specification

- 4.1** The registration will be granted in Form IA stamped with an authorized seal indicating so.

- 4.2** The temporary registration will be granted for duration of three months at a time with a maximum of six months.

5.0 FEES FOR REGISTRATION

The fees for registration of medicinal products are specified in part XXI of the Rules and Regulation and will be subjected to revision from time to time.

Processing fee/Token fee

Every application for registration should be accompanied with a processing fee of Nu. 150.00(equivalent to INR 150.00) per product.

Registration fee

The registration fee of Nu. 1500.00 per product should be paid at the time of issuance of registration certificate.

Temporary registration fee

The temporary registration fee of Nu. 500.00 per product should be paid at the time of issuance of registration certificate.

5.1 Mode of payment: The payment in demand draft maybe made in favour of DRA, Ministry of Health, Thimphu Bhutan.

Any payment made is **not** refundable once an application has been submitted and payment confirmed. Applications without the correct fees will not be processed.

Guidelines for application for Registration of Medicinal Products 2006(DRA)

5.2 Multiple Applications

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

6.0 PROCESSING OF APPLICATIONS

Initiation of Review

Review of applications will follow a queue system.

Priority review may be granted where the product is intended for treatment of a serious or public health emergencies (Fast track registration).

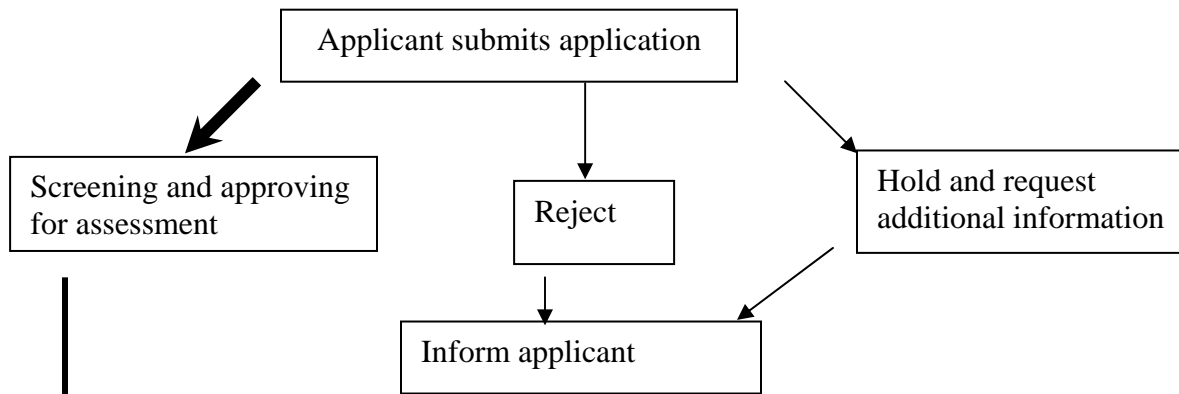
Stop Clock

The clock starts once payment has been confirmed for a submitted application and will stop whenever the DRA needs to seek further information from the applicant. The clock restarts when the DRA receives complete responses from the applicant. A period of **3 months** will be given within which the applicant should submit the additional information/clarification required for each correspondence from the DRA.

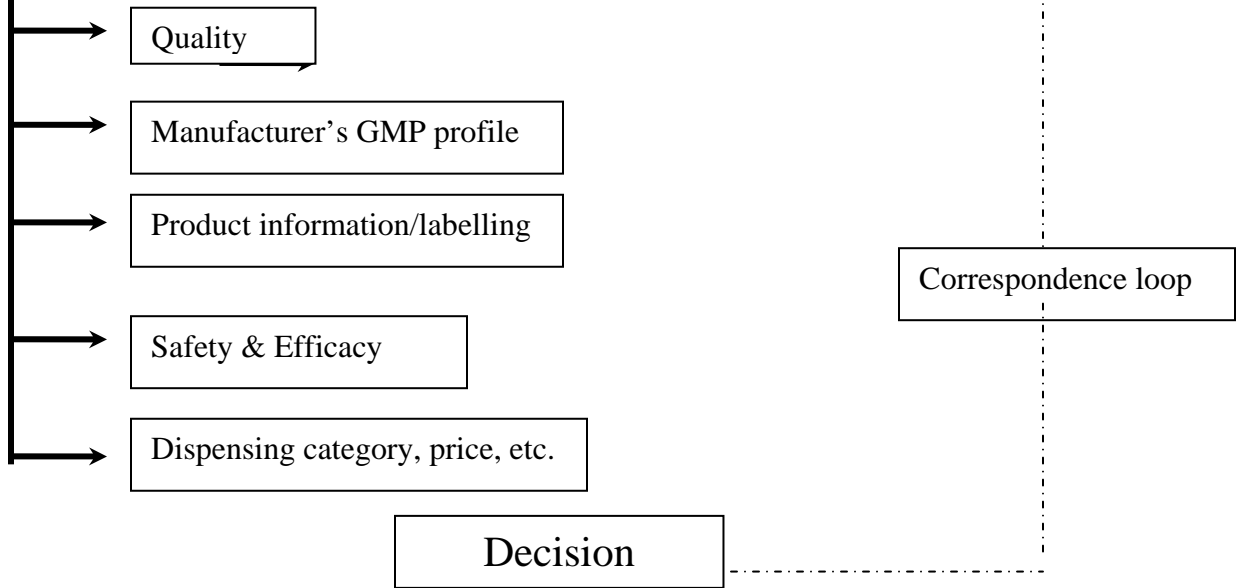
The clock stops when the DRA informs the applicant of its regulatory decision.

6.1 Assessment of Applications for Market Authorization

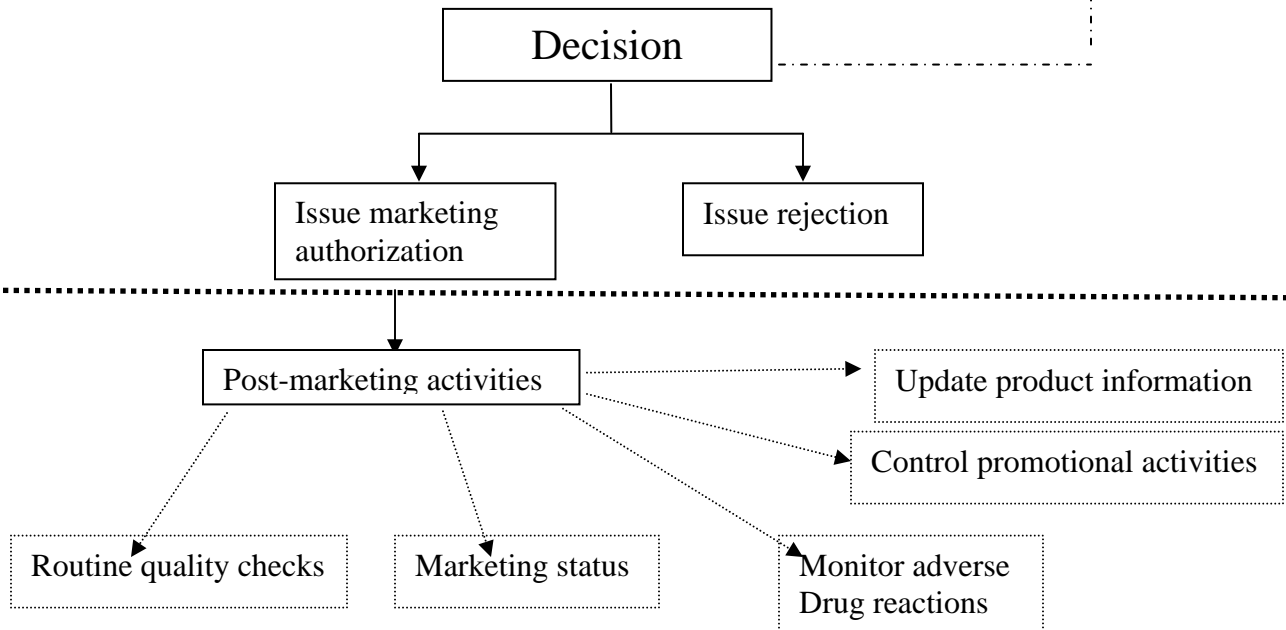
RECEPTION



ASSESSMENT



FOLLOW-UP



Guidelines for application for Registration of Medicinal Products 2006(DRA)

7.0 REGULATORY OUTCOME

7.1 Decisions of the Board

A regulatory decision is made based on the outcome of the evaluation of the submitted documentation. The board may, in the interest of public safety, reject the registration of any product prior to submitting for approval from Board. The decision will be notified to the party.

7.2 Product Registration Number

A registration number will be allocated by the Authority when a product application is deemed to have satisfied the registration requirements. The registration number is specific for the product registered with the name, identity, composition, characteristics, origin (manufacturer) and marketing authorization holder. It may NOT be used for any other product.

7.3 Award of registration certificate

- The registration certificate will be issued in Form IA of Bhutan Rules & Regulation 2005
- The registration certificate will be issued within 30 working days from the date of receipt of complete documents unless otherwise a longer period is required in case of which the party will be notified.

7.4 Validity Period of Registration

The registration of a product should be valid for a period of three years and should be specified in the certificate.

7.5 Renewal of registration

- Application for renewal should be made before three months from the date of expiry of registration.
- A grace period will extend to one month after the specified expiry date.
- Defaulter will pay a penalty of Nu. 100 per day after the expiry of grace period up to one month.

7.6 Cancellation of registration

The Board should authorize the Authority to cancel the registration of any product if:

- i. The composition of the product has been changed or

Guidelines for application for Registration of Medicinal Products 2006(DRA)

- ii. Any of the conditions of registration of the product has been contravened or changed, or
 - iii. Any report on adverse drugs reactions of serious nature have been received from National Pharmacovigilance Centre or any other national or international sources, or
 - iv. The information which was furnished at the time of application is later found to be false or insufficient.
- iii. Defaulting of timely renewal beyond one month after grace period, or
- iv. For any other matters as specified by the Board at the time of cancellation.

8.0 APPEAL AGAINST DRA/DTAC DECISIONS

Any applicant/marketing authorization holder aggrieved by the decisions of the DRA/DTAC may make a written appeal to the Bhutan Medicines Board. **All notice of appeals must be made within thirty (30) days** from the date of the DRA notification.

8.1 Change in particulars of registered products

No change in product name, product specifications, packing, indications, contents of product label, package insert, or product literature, or any relevant particulars of the registered product should not be made without the prior approval of the Board.

The registration of a product may be cancelled if changes are made without the prior approval of the Board.

Any change which affects the composition or characteristics of the product such as colour/shade, flavour/fragrance, shape, change of vehicle (liquid preparation) should require a new application for registration.

9.0 OTHER INFORMATION

9.1 Criteria for registration

A product will be registered only if it satisfies **all** requirements of the DRA, especially **with respect to safety, efficacy and quality** of the product.

Other criteria that may be taken into consideration include:

- i. Either that the product is needed or not. Aspects like potential for abuse, number of registered products, different dosage form, etc are considered;
- ii. Therapeutic advantage.

Guidelines for application for Registration of Medicinal Products 2006(DRA)

9.2 Combination Packs

Products which are in combination packed together for a therapeutic regimen (example for the treatment of Helicobacter Pylori, Hepatitis C, etc.) will be classified as a Combination Pack Product and should be registered as a single product.

A product which is packed together with diluent(s) is not considered as Combination Pack Product.

9.3 Product Label(should be either in English or Dzongkha(national language))

The following information should be present on the labeling of the product

Outer label:

- a. Name of product
- b. Dosage Form
- c. Name and address of manufacturer or marketing authorization
- d. Name of the Active Substance(s)
- e. Manufacturing License no.
- f. Batch No. of product.
- g. Storage Condition
- h. Manufacturing date and Expiry date

Inner label:

1. Individual name for each product or Name of combination pack
2. Name of the Active Substance(s)
3. Individual Batch No. for each product
4. Name and address of manufacturer
5. Individual expiry date for each product

* Exempted for small label such as ampoule and vial