

GUIDELINE ON APPLICATION TO AMEND MANUFACTURING LICENCE OF MEDICINAL PRODUCTS

1. INTRODUCTION

All medicinal products manufactured, sold, supplied or imported into Brunei Darussalam are regulated under the Medicines Order, 2007. A company with an existing Manufacturing Licence may apply for an amendment to any particulars in the licence including the list of manufactured products attached to the licence.

2. SCOPE

This Guideline is intended to provide assistance in the submission of application for amendment of a manufacturing licence of medicinal products.

3. APPLICATION PROCEDURE

3.1 An application to amend a manufacturing licence of medicinal products shall be submitted by filling in form no.: BDMCA/DPS/MLV/14 – *Application to Amend Manufacturing Licence of Medicinal Products*.

3.2 The form must be typed. Only **ONE ORIGINAL COPY** of the completed application form is required to be submitted.

3.3 All sections of the application form must be completed. Please indicate N.A. (Not applicable) in those sections that are not relevant to the application.

3.4 Only completed application form with payment will be processed.

4. MODE OF PAYMENT

4.1 Fee for application to amend a licence:

- | | | | |
|----|---|---|-------|
| a. | with site inspection (for manufacturer) | - | \$100 |
| b. | with site inspection (for assembler) | - | \$50 |
| c. | without site inspection | - | \$25 |

4.2 Payment of fees for application to amend a manufacturing licence of medicinal products can either be made in the forms of **cash** or **cheque** only and are **non-refundable**. Payments by cheque shall be made payable to “Kerajaan Brunei” or “**Government of Brunei**”.

5. APPLICATION FORM

Section 1: Instructions

Please refer to Section 1 for instructions on filling in the application form.

Section 2: Checklist for Supporting Documents

The checklist in this section is to be filled in by the applicant. The list of supporting documents indicated is to be submitted together with the application form.

Section 3: Company Particulars

The company name and address in this section should be the same as appear in the current manufacturer's licence.

Section 4: Applicant Particulars

The applicant must be the holder of the current Manufacturer Licence. The person named in this section should be based in Brunei Darussalam and be contactable at all times. The Department of Pharmaceutical Services (DPS) will only liaise with this person pertaining to the application and inspection arrangements.

Section 5: Details of Amendment

For amendments of a licence to manufacture medicinal products, the Applicant is required to complete **Section 5.1 (a)** of the form and provide information on the amendment details such as type of amendment, current details, proposed changes and expected effective date, and the reason for the amendment. The list of document to support each of the proposed changes must also be provided.

For amendments to list of medicinal products, this section requires the applicant to provide information if there is an amendment to the list of medicinal products the company is dealing with. All products manufactured at the facilities must be registered or notified with the Ministry of Health, Brunei Darussalam. The applicant is required to complete **Section 5.2(a)** of the form and provide information on the amendment to the list of Medicinal Products such as the Product name with the active ingredient and strength, pack size, Product Licence number (if applicable) and the validity period.

Details on the *types of amendment* and *supporting documents* required are shown in Table 1.

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Table 1: Types of Amendment to a Manufacturing Licence of Medicinal Products

No.	Types of Amendment	Supporting Documents	Site Inspection
1.	Change of manufacturing site	Site Master File	Required
2.	Inclusion of new or change of storage site location/address for the storage of starting materials, packaging materials, intermediate products or finished products of concern	Site Master File	Required
3.	Manufacturing or primary assembly of a new dosage form which may involve the use of different technology and expertise (equipment, processes)	<ul style="list-style-type: none"> • Site Master File • List of manufacturing equipment available and their function, if applicable. • A copy of Product Licence and/or Letter of Approval for Variations to a Registered Medicinal Product, if applicable. 	Required
4.	Manufacturing or primary assembly of a new category of product comprising highly sensitizing materials, biological preparations containing living organisms or highly active materials. E.g. such materials including but not limited to penicillins, cephalosporins, hormones, steroids and cytotoxic substances	<ul style="list-style-type: none"> • Site Master File • List of manufacturing equipment and their function, if applicable. • A copy of Product Licence and/or Letter of Approval for Variations to a Registered Medicinal Product, if applicable 	Required
5.	Secondary assembly of preparations containing cytotoxic substances or biologicals preparations containing living organisms or viruses	<ul style="list-style-type: none"> • Site Master File • List of manufacturing equipment available and their function, if applicable. 	Required
6.	Deletion of existing manufacturing site and warehouse	Nil	NOT Required
7.	Secondary assembly of a new dosage form (other than preparations containing cytotoxic substances or biologicals preparations containing living organisms or viruses)	<ul style="list-style-type: none"> • Site Master File • List of manufacturing equipment available and their function, if applicable. 	NOT Required
8.	Deletion of approved dosage form for manufacturing, primary assembly and secondary assembly	Nil	NOT Required
9.	Change of company particulars such as company name or address	A copy of Company / Business Certificate of Registration (Section 16 & 17)	NOT Required
10.	Change to the list of medicinal products company is manufacturing	<ul style="list-style-type: none"> • List of medicinal products manufactured 	NOT Required
11.	Change of applicant	<ul style="list-style-type: none"> • Letter of authorisation from company 	NOT Required

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12	Change of key personnel / responsible person	<ul style="list-style-type: none"> • Site Master File • Letter of authorisation from company 	NOT Required
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Note: While some of the above changes do not require a site inspection, the Authority reserves the right to make the final decision and a site inspection may be conducted.

Examples of changes involving site inspection are as follows:

- Inclusion of new or change of manufacturing site location/address for the type of production operations (including the type of products and/or dosage forms) being conducted when the new site has not been audited or approval by the DPS yet.
- Inclusion of new or change of storage site location/address for the storage of starting materials, packaging materials, intermediate products or finished products of concern when the new site has not been audited or approval by the DPS yet.
- Inclusion of new or change of manufacturing site location/address when the new site has not been audited or approval by the DPS yet for quality control testing operations as regards the manufacture of the medicinal products of concern.
- Transfer of the manufacture of an aseptically processed sterile product to (a) a newly constructed or refurbished aseptic processing facility or areas or (b) an existing or aseptic processing facility or area that does not manufacture similar (including container types and sizes) approved products. (Note: A change in location for terminal sterilization would be assessed in the next routine audit. The proposed room design and classification should be similar to the approved specification\).
- Manufacturing or primary assembly of a new dosage form which may involve the use of different technology and expertise (equipment, processes).
- Manufacturing or primary assembly of a new category of product comprising highly sensitizing materials, biological preparations containing living organisms, or highly active materials. E.g. of such materials include but not limited to penicillin, cephalosporins, hormones, steroids and cytotoxic substances or biologicals preparations containing living organisms or viruses.

Examples of changes that do not involve site inspection are as follows:

The appropriateness of such changes would be assessed in the next inspection. While the following generally do not require an inspection, the authority reserves the right to make the final decision and a site inspection may be conducted.

- Construction activities at a manufacturing site or moving production operations within a building or between buildings at the same manufacturing site (without any change in the address(es) as approved on the licence)
- Changes to an approved operation (eg addition, deletion or substitution of processing steps, replacement of machinery)
- Deletion of existing manufacturing site and warehouse
- Secondary assembly of a new dosage forms (other than preparations containing cytotoxic substances or biologicals preparations containing living organisms or viruses)
- Deletion of approved dosage form for manufacturing, primary assembly and secondary assembly
- Change of applicant
- Change of personnel in-charge of production and quality control

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- Change of contract testing laboratories
- Change of company particulars such as company name or address.

Section 6: Declaration of Applicant

Application form must be declared and signed by the applicant.

Section 7: Certification (Company/Establishment)

This section must be filled in by the Company's Owner / Manager / Director in cases where the changes in the applicant's particular who is authorised by the company who is not the Owner/ Manager/ Director of the company.

6. For any enquiries related to the application please contact:

Product Regulation Section
Department of Pharmaceutical Services
Ministry of Health
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Brunei Darussalam
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