

**DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG EVALUATION AND IMPORT/EXPORT CONTROL DIVISION**

**Guidance Notes on Change of Registered Particulars
of Registered Pharmaceutical Products/Substances**

Registered particulars of a registered pharmaceutical product/substance

1. According to the Pharmacy and Poisons Regulations (Cap. 138A), the following particulars of a registered pharmaceutical product/substance are also registered with the Pharmacy and Poisons Board:
 - (a) the name of the pharmaceutical product/substance;
 - (b) the specifications of the pharmaceutical product/substance;
 - (c) the label of the pharmaceutical product/substance;
 - (d) the package insert of the pharmaceutical product/substance, if any;
 - (e) the name and address of the manufacturer;
 - (f) the name and address of the registration certificate holder;
 - (g) the dose form of the pharmaceutical product;
 - (h) the quantity or quantities of the dose form contained in the unit package or unit packages of the pharmaceutical product;
 - (i) the name and quantity of all active ingredients of the pharmaceutical product;
 - (j) the name and quantity of all excipients of the pharmaceutical product; and
 - (k) the proposed indication, dosage and route of administration of the pharmaceutical product.

Change of registered particulars

2. A pharmaceutical product/substance is registered if and only if none of the above registered particulars has been changed without approval. If any one of the above particulars has been changed without approval, the product/substance will not be regarded as registered under the Pharmacy and Poisons Regulations.
3. Applications for change of any registered particulars, except the items underlined in paragraph 1 (i.e. the name of product/substance, the dose form, and active ingredients), must be made following this Guidance Notes.
4. The items underlined in paragraph 1 cannot be changed. Such change will result in the product/substance being considered as a new pharmaceutical product/substance, and new application for registration is required. For details, please refer to the “Guidance Notes on Registration of Pharmaceutical Products/Substances”.

How to apply for change of registered particulars?

5. Applications for change of registered particulars should be submitted online via the Pharmaceutical Registration System 2.0 (PRS 2.0) at:

https://www.drugoffice.gov.hk/prs2-ext/client_authentication.jsp

Applicants should provide the supporting document(s) as indicated in the table on the following pages in Portable Document Format (PDF). The original or certified true copies of supporting documents, such as the manufacturer's Good Manufacturing Practice (GMP) certificate, free sale certificate and Certificate of a Pharmaceutical Product, should be submitted to the following address with the application reference number (i.e. CORP-HKXXXXXX-XXXXXXXXXX) and date of online submission indicated in the cover page:

Drug Registration Unit
Drug Evaluation and Import/Export Control Division
Drug Office, Department of Health
Suites 2002-05, 20/F, AIA Kowloon
Tower, Landmark East, 100 How
Ming Street, Kwun Tong, Kowloon
(Enquiries by telephone: 3974 4175)

6. **In addition to the supporting documents as specified in Table 1, other relevant supporting documents may be required to substantiate the safety, efficacy and quality of the pharmaceutical product/substance with its proposed change(s).**
7. **Applications with inappropriate data entry, irrelevant supporting documents or documents which do not conform to these Guidance Notes will be not be accepted and deficiency letters will be sent to applicants via PRS 2.0 for further action.**

Important Note: If the product/substance is supplied to the Department of Health via tender or direct purchase agreements, please indicate in the application in the PRS 2.0.

Approval

8. If the application is approved, the applicant will be informed of the approval in writing and effective date of the proposed change(s). In general, the default effective date of the proposed change(s) will be 180 days from the date of approval if no implementation date is proposed in the application.

9. Prior to the effective date of the proposed change(s), the applicant should recall all products/substances with the old particulars from the market. As stated in paragraph 2, these products/substances will no longer be regarded as registered pharmaceutical products/substances on or after the effective date.

Fees

10. In general, no fees are charged. However, for the change of the name or address of registration certificate holder, a signature fee (currently \$155 per certificate) will be charged for each registration certificate.

Table 1: Supporting Documents for Change of Registered Particulars:

Proposed Change(s)	Requirements of Supporting Document(s)
1. Name of Product/Substance	None - New application for registration is required
2. Specifications	
a. Change in specification(s)	Proposed specifications [!] , clean copy and with the change(s) underlined or highlighted
b. Change in shelf-life or container closure system	<ul style="list-style-type: none"> i. Stability test data [^] ii. Proposed specifications [!], clean copy and with the change(s) underlined or highlighted iii. Proposed label and package insert, clean copy and with the change(s) underlined or highlighted, if applicable
c. Change in storage condition	<ul style="list-style-type: none"> i. Stability test data [^] ii. Proposed specifications [!] and label, clean copy and with the change(s) underlined or highlighted iii. Proposed package insert, clean copy and with the change(s) underlined or highlighted, if applicable
3. Label	
a. Change in label [^]	Proposed label, clean copy and with the change(s) underlined or highlighted
4. Package Insert	
a. Change in package insert	<ul style="list-style-type: none"> i. Proposed package insert, clean copy and with the change(s) underlined and highlighted ii. Documents substantiating the proposed change(s) with the relevant sections highlighted
b. Addition of package insert	<ul style="list-style-type: none"> i. Proposed package insert, clean copy ii. Documents substantiating the proposed package insert with the relevant sections highlighted
5. Manufacturer [♦]	
a. Change in name and/or address of the current manufacturer	<ul style="list-style-type: none"> i. Soft copy and original/certified true copy of the manufacturer's GMP certificate [#] ii. Proposed label ^θ, clean copy and with the change(s) underlined or highlighted iii. Proposed package insert, clean copy and with the change(s) underlined or highlighted, if applicable iv. Updated master formula [!] issued by the manufacturer with the new name and/or address, if applicable v. Updated specifications [!] issued by the manufacturer with the new name and/or address, if applicable

Table 1: Supporting Documents for Change of Registered Particulars (cont'd):

Proposed Change(s)	Requirements of Supporting Document(s)
b. Change to new manufacturer	<ul style="list-style-type: none"> i. Soft copy and original/certified true copy of the manufacturer's GMP certificate # ii. Soft Copy and original/certified true copy of free sale certificate of the product/substance issued by the health authority of the country of origin ^θ (for change of country of origin only) iii. Proposed label ^θ, clean copy and with the change(s) underlined or highlighted iv. Proposed package insert, clean copy and with the change(s) underlined or highlighted, if applicable v. Letter issued by the current manufacturer to acknowledge the change to the new manufacturer vi. Updated master formula [!] ^θ issued by the new manufacturer vii. Updated specifications [!] ^θ issued by the new manufacturer
6. Registration Certificate Holder	
a. Change in name and/or address of the current registration certificate holder	<ul style="list-style-type: none"> i. Soft copy of the amended business registration certificate ii. Soft copy of the Certification of Incorporation on the Change of Name (for incorporated companies only) iii. Original Certificate(s) of Drug/Product Registration of all registered pharmaceutical product(s)/substance(s)
b. Change to new registration certificate holder	<ul style="list-style-type: none"> i. Letter from the current registration certificate holder agreeing to transfer the named registered pharmaceutical products/substances to the new registration certificate holder ii. Letter from the new registration certificate holder agreeing to accept the named registered pharmaceutical products/substances iii. Letter from the current manufacturer confirming the transfer and naming the registered pharmaceutical products/substances to be transferred iv. Original Certificate(s) of Drug/Product Registration of all registered pharmaceutical product(s)/substance(s) v. Soft copy of the business registration certificate of the new registration certificate holder
7. Dose Form	None - New application for registration is required
8. Quantity / Quantities of the Dose Form in the Unit Package(s) (i.e. Package Size)	
a. Change in package size	<ul style="list-style-type: none"> i. Proposed label, clean copy and with the change(s) underlined or highlighted ii. Proposed package insert, clean copy and with the change(s) underlined or highlighted, if applicable iii. Proposed specifications [!], if applicable iv. Stability test data ^Δ

Table 1: Supporting Documents for Change of Registered Particulars (cont'd):

Proposed Change(s)	Requirements of Supporting Document(s)
b. Addition of package size	i. Proposed label, clean copy ii. Proposed package insert, clean copy and with the changes(s) underlined or highlighted, if applicable iii. Proposed specifications [!] , if applicable iv. Stability test data [^]
9. Name and Quantity of Active Ingredients	None - New application for registration is required
10. Excipients	
a. Change in name and/or quantity of excipients	i. Proposed master formula [!] , clean copy and with the change(s) underlined or highlighted ii. Proposed specifications [!] iii. Stability test data [^]
11. Indication / Dosage / Route of Administration	
a. Change in indication [*]	i. Proposed label and/or package insert, clean copy and with the change(s) underlined or highlighted ii. Approval from health authorities or documents substantiating the proposed change(s) with the relevant sections highlighted
b. Change in dosage [*]	i. Proposed label and/or package insert, clean copy and with the change(s) underlined or highlighted ii. Approval from health authorities or documents substantiating the proposed change(s) with the relevant sections highlighted
c. Change in route of administration [*]	i. Proposed label and/or package insert, clean copy and with the change(s) underlined or highlighted ii. Approval from health authorities or documents substantiating the proposed change(s) with the relevant sections highlighted

Abbreviations:

- [!] Please refer to the “General Requirements for Master Formula and Specifications for Non-Biological Products” in Appendix One.
- [^] For addition of new presentation(s) of a registered pack size, a new application for registration is required.
- ◆ (1) “Manufacturer” as defined under the Pharmacy and Poisons Ordinance (Cap. 138).
(2) For addition of new source(s), a new application for registration is required.
- # The manufacturer must comply with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP standards.
- ⊖ For applications involving the change of manufacturer appeared on the label.
- ^{*} For any proposed change(s) in indication/dosage/route of administration which has not been previously registered in Hong Kong, clinical data to support the proposed change(s) and worldwide approval status in reference countries are generally required.

△ Stability test data should be done at one of the following Temperature (°C) / Relative Humidity (RH) conditions:

- Other temperature / relative humidity conditions could be adopted where justified;
- Appropriate labelling of storage conditions in English and/or Chinese should be provided on the sales pack.

Real Time Testing Conditions	
(i)	30°C±2°C / 75%±5% RH
(ii)	30°C±2°C / 65%±5% RH
(iii)	25°C±2°C / 60%±5% RH
Accelerated Testing Conditions **	
(iv)	40°C±2°C / 75%±5% RH for 6 months

** At least 3 months' real time stability test data must also be provided.

Appendix One

General Requirements for Master Formula and Specifications for Non-Biological Products

Master Formula

The following information should be included in the master formula of a pharmaceutical product (PP):

- (a) name of the product;
- (b) description of the dose form;
- (c) strength of the product;
- (d) name(s) of all active ingredient(s) and the amount on a per-unit basis;
- (e) list of all excipients with the following information:
 - their non-proprietary names;
 - their amount on a per-unit basis;
 - their functions; and
 - colour index numbers or E-numbers for all the colourants used (including capsule shells), if applicable; and
- (f) overage with justification, if applicable.

Master formula of a PP should be issued by the manufacturer of the product. The certificate holder may include the appropriate references on quality standards of the active ingredients and excipients (e.g. pharmacopoeial monographs or manufacturer's in-house specifications).

Questions and Answers on the Master Formula:

1. What are the particular requirements for the change of excipients of a PP?

In general, the certificate holder is required to provide the proposed master formula, specifications, and stability reports to support the application for the change of excipients of a PP. Process validation reports may be required when applicable. When the application is related to minor variation of excipient(s) and is supported by justifications, process validation reports may not be required.

2. Is it required to include the overage of active ingredient in the master formula?

If there is overage of active ingredient, the information should be included in the master formula of the registered PP. Hence, any change of overage of active

ingredient in the master formula shall require prior approval for change of registered particulars of the PP (i.e. CORP application).

3. When a substance (e.g. alcohol as solvent) is used in the manufacturing process but would not be detected in the final product, is the information required to be included in the master formula?

In general, when a substance is used in the manufacturing process but would not be detected in the final product (e.g. alcohol used in granulation of a solid dose form will be evaporated during the manufacturing process), the information is not required to be included in the master formula; but should be clearly recorded in other manufacturing documents (e.g. manufacturing process and records).

4. If there is a change in the quality standard of active ingredients or excipients, is CORP application required?

If the quality standard of active ingredients or excipients has been stated in the master formula of the registered PP, then CORP application and statutory approval are required for change of quality standard of the ingredients (e.g. from BP to USP quality standard).

5. If there is a change in the form of active ingredient of a registered PP, is CORP application required?

Physical form of the active ingredient is not required to be stated in the master formula. However, if the specific physical form of the active ingredient is stated in the master formula of a registered PP, then CORP application and prior approval are required for any change of the physical form of the active ingredient.

6. How should the names and quantities of active ingredients and excipients be expressed in the master formula?

The names of the ingredients should be expressed by either the names in the Poisons List as stipulated in the Pharmacy and Poisons Ordinance or the World Health Organization (WHO)'s international non-proprietary names (INNs) in the master formula. Besides, the quantities of the ingredients should be expressed on a per-unit basis in the master formula.

Meanwhile, applicants should refer to the Pharmacy and Poisons Ordinance and Regulations for the legal requirements on labelling of pharmaceutical products, including the names and quantities of the active ingredients.

Specifications

The following information should be included in the specifications of a PP:

- (a) name of the product;
- (b) description of the dose form;
- (c) the relevant tests for final release of the finished product and their acceptance criteria;
- (d) *type of container and closure of the product;
- (e) *storage conditions and any special handling precautions, if applicable; and
- (f) *shelf-life of the product.

(* Note: A declaration can be made by the applicant stating that the information on the type of container, closure system, storage conditions or shelf-life of the product have been provided in separate documents inside the dossier and will form part of the specifications.)

Questions and Answers on the Specifications:

1. What general tests should be included in the specifications of a PP?

The following tests are generally required:

- (a) physical description (e.g. size, shape, color, etc.);
- (b) identification of the active ingredient;
- (c) assay of the active ingredient; and
- (d) impurities, if applicable.

Note: Specific tests may be required in the specifications for different products. Certificate holders should refer to the appropriate pharmacopoeial or reputable references (e.g. ICH and WHO guidelines) for details of the relevant tests and their corresponding requirements.

2. Is CORP application required for change of method of analysis?

Method of analysis is not a registered particular, but is required in the application for registration of a PP. Therefore, change of method of analysis of the PP should be provided to DH Drug Office for record purposes. Besides, certificate holder is reminded to comply with the “change control” GMP requirements, if applicable.