Guidance Notes on Registration of Pharmaceutical Products/Substances

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Pharmacy and Poisons Board of Hong Kong

Contents

1. Preface

1.1 These Guidance Notes outline the general requirements for registration of pharmaceutical products and should be read in conjunction with the current laws governing pharmaceutical products in Hong Kong, which include the following Ordinances and their relevant subsidiary legislation:

- Pharmacy and Poisons Ordinance (Chapter 138);
- Antibiotics Ordinance (Chapter 137);
- Dangerous Drugs Ordinance (Chapter 134);
- Undesirable Medical Advertisements Ordinance (Chapter 231);

1.2 If there is any inconsistency between these Guidance Notes and the legislation, the latter shall prevail. Applicants are strongly encouraged to familiarize themselves with the content of these Guidance Notes before submitting their applications.

2. Pharmaceutical products subject to registration

2.1 Under the Pharmacy and Poisons Regulations, pharmaceutical products must be registered with the Pharmacy and Poisons Board of Hong Kong before they can be sold, offered for sale, distributed or possessed for the purposes of sale, distribution or other use. The Drug Office of the Department of Health is responsible for providing executive and professional support to the Pharmacy and Poisons Board in drug registration matters.

Pharmaceutical product —

(a) means a substance, or combination of substances that —

(i) is presented as having properties for treating or preventing disease in human beings or animals; or

(ii) may be used in or administered to human beings or animals with a view to –

(A) restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action; or

(B) making a medical diagnosis; and

(b) includes an advanced therapy product.

2.2 In considering whether or not your product is a "pharmaceutical product", please refer to the <Guidance Notes on Classification of Products as "Pharmaceutical Products" under the Pharmacy and Poisons Ordinance (Cap. 138)>. You should take into account of the composition of your product and the nature of the claims you make in relation to the product. In general, if your product contains a drug substance in its composition, or if it carries "medicinal" claims in its label, leaflet, brochure, wrapper, advertisements and other promotional materials, it will fall within the definition of pharmaceutical product and registration is required. Products commonly referred to as cosmetics, toiletries and disinfectants which do not contain any drug ingredient in their composition and which are sold without any medicinal claims may be excluded. Accordingly, it is your obligation to have complete knowledge of your product. If it falls within the definition of pharmaceutical product, you might commit an offence of the sale of an unregistered pharmaceutical product unless it has been registered with the Pharmacy and Poisons Board.

2.3 For advanced therapy product (ATP) applications, please refer to the <Guidance on Application of Certificate of Drug / Product Registration — Advanced Therapy Products>;

3. Pharmaceutical products not subject to registration

3.1 Products or drug substances which fall under the following categories are not required to be registered with the Pharmacy and Poisons Board:

3.1.1 containing only proprietary Chinese medicines or Chinese herbal medicines as defined in the Chinese Medicine Ordinance (Cap. 549);

3.1.2 imported by licensed manufacturers solely for the purpose of manufacturing their own pharmaceutical products;

3.1.3 possessed or used under the direction of a registered medical practitioner or a registered dentist for the treatment of a particular patient, or of a registered veterinary surgeon for the treatment of a particular animal;

3.1.4 imported for re-export only;

3.1.5 manufactured in Hong Kong for export by the licensed manufacturer only;

3.1.6 administered for the purposes of a clinical trial/medicinal test in accordance with a clinical trial/medicinal test certificate issued under the Pharmacy and Poisons Regulations.

4. Criteria for registration

4.1 Your pharmaceutical product will only be approved for registration if it meets the criteria of safety, efficacy and quality relevant to it.

5. Who should apply

5.1 If your pharmaceutical product is manufactured in Hong Kong, the person responsible for obtaining registration of the product is the licensed manufacturer, or the licensed wholesale dealer contracting with the licensed manufacturer.

5.2 If your pharmaceutical product is manufactured outside Hong Kong, the person responsible for obtaining registration is the licensed wholesale dealer who imported the pharmaceutical product, or the Hong Kong branch, subsidiary, representative, agent or distributor of the overseas manufacturer.

6. How to apply

6.1 You should submit your application for registration of pharmaceutical product via the online Pharmaceuticals Registration System 2.0 (PRS 2.0) of Drug Office of the Department of Health at https://www.drugoffice.gov.hk/prs2-ext/client_authentication.jsp together with the following:

6.1.1 The application fee, currently at $1,100 (Please also see paragraph 9 below), to be paid via PRS 2.0 with credit card/PPS online payment services, or in person by cash or cheque along with the notification of payment at the following address:

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,

Hong Kong (Enquiries: 3974 4175)

6.2 The following particulars in text searchable Portable Document Format (PDF) file:

6.2.1 electronic copy of the business registration certificate of the applicant;

6.2.2 an authorization letter from the manufacturer/marketing authorization holder, authorizing the applicant to apply the registration for its product;

6.2.3 a letter of authorization signed by the applicant (sole-proprietor, managing partner or director) and stamped with the applicant's company chop to authorize a person (with relevant contact telephone, facsimile numbers and email address) to handle the application on its behalf and the applicant should also undertake it "agrees to submit additional or updated supporting documents at any stage of registration when required";

6.2.4 electronic copy (Please also see paragraph 6.3 below) of the manufacturer(s)' licence;

6.2.5 electronic copy (Please also see paragraph 6.3 and 8.3 below) of Good Manufacturing Practices (GMP) certificate of the manufacturer(s), with evidence of compliance to the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP standards. For details, please refer to the <Questions and Answers on PIC/S GMP Requirements for Registration of Imported Pharmaceutical Products>;

6.2.6 for application relating to a pharmaceutical product manufactured outside Hong Kong, the methods, standards and conditions of the manufacture of the pharmaceutical product will also be taken into consideration. Applicants should therefore submit detailed information regarding the overseas manufacturer(s), including the manufacturing and quality control facilities and technical personnel, etc. (e.g. site master file);

6.2.7 electronic copy (Please also see paragraph 6.3 below) of Free Sale Certificate or Certificate of a Pharmaceutical Product (CPP) of the product. The certificate should be issued by the drug regulatory authority of the country of origin unless otherwise justified;

6.2.8 description and composition of the finished product issued by the manufacturer. Please refer to the <General Requirements for Master Formula and Specifications for Non-Biological Products>;

6.2.9 release specification and shelf-life specification (if applicable) of the finished product issued by the manufacturer. Document(s) showing compliance with one or more of the following pharmacopoeias or ICH / WHO guidelines must be provided unless otherwise justified: Pharmacopoeia of the People's Republic of

China, British Pharmacopoeia, European Pharmacopoeia, International Pharmacopoeia, Japanese Pharmacopoeia and/or United States Pharmacopoeia. Please refer to the <General Requirements for Master Formula and Specifications for Non-Biological Products>;

6.2.10 detailed method of analysis of the product for all tests stated in the finished product specifications;

6.2.11 certificate of analysis of a representative batch of the finished product issued by the manufacturer or the company performing the analysis;

6.2.12 stability test data of the product. Completed real time stability data at one of the following real time testing conditions, or on-going real time stability data together with at least 6 months' accelerated stability data and commitment to provide completed stability data is required to establish the product's shelf-life. In-use stability data should also be provided if applicable.

Real Time Testing Condition

Temperature (°C)		Relative humidity (RH)
● 30°C+/-2°C	&	75%+/-5% RH
● 30°C+/-2°C	&	65%+/-5% RH
● 25°C+/-2°C	&	60%+/-5% RH

Accelerated Testing Condition

● 40°C+/-2°C	&	75%+/-5% RH

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

6.2.13 one set of prototype sales pack (e.g. outer carton, container label, and other component(s) comprising the sales pack) and proposed package insert (if any) for each applied pack size of the product. Please refer to the <Guidelines on the Labelling of Pharmaceutical Products>;

6.2.14 colour photos or scanned image of the product, including any inner container/packaging and the unit dose form image of the product sample, clearly

showing the complete content of the prototype sales pack and its component(s), for examples:

- the colour and engraving/printing of a tablet/capsule;
- the colour of liquid or semi-solid dosage forms (e.g. syrup, suspension, linctus, cream, ointment);
- the colour and shape of suppositories/pessaries, etc.;
- the shape and appearance of the container;

6.2.15 clinical and scientific documentation substantiating the safety and efficacy of the product:

6.2.15.1 for generic product applications which their originator products have been registered in Hong Kong for over 8 years, please see paragraph 6.2.16 & 6.2.17 below;

6.2.15.2 for products containing a new chemical or biological entity (NCE), or for products which no previously registered reference products could be identified in Hong Kong, please refer to the <Guidance Notes on Registration of Pharmaceutical Products Containing a New Chemical or Biological Entity>;

6.2.15.3 for biosimilar product applications, please refer to the <Guidance Notes on Registration of Biosimilar Products>;

6.2.16 the following document(s) to support the proposed indication(s), dosage, route of administration and other contents of the package insert (if any):

- copy of reputable references (e.g. American Hospital Formulary Service Drug Information, British National Formulary, Medicines Compendium, Drug Information Handbook, Drug Facts and Comparisons, Martindale The Complete Drug Reference or Physicians' Desk Reference); and/ or

- approved package insert (with evidence of approval) from the drug regulatory authority of one of the following countries: Australia, Austria, Belgium, Bulgaria, Canada, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Holland, Hungary, Ireland, Italy, Japan, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, UK and USA;

Cross-referencing to documents should be made by referring to the page number of the reference documents and the relevant parts of the reference documents should be highlighted clearly;

6.2.17 bioequivalence (BE) data:

- for anti-epileptic drugs which include Carbamazepine, Clobazam, Clonazepam, Clorazepate, Divalproex, Ethosuximide, Ethotoin, Felbamate, Fosphenytoin, Gabapentin, Lamotrigine, Lacosamide, Levetiracetam, Mephenytoin, Mesuximide, Oxcarbazepine, Pheneturide, Phensuximide, Phenytoin, Pregabalin, Primidone, Rufinamide, Sultiame, Tiagabine, Topiramate, Trimethadione, Vigabatrin, Valproates and Zonisamide;

- for critical dose drugs/ narrow therapeutic range drugs which include Acetohexamide, Aminophylline, Aprindine, Chloramphenicol, Choline theophylline, Clindamycin, Clonidine, Cyclosporine, Digitoxin, Digoxin, Diprophylline, Disopyramide, Ethinyl Estradiol, Flecainide, Glibenclamide, Gliclazide, Glybuzole, Glyclopyramide, Guanethidine, Isoetharine, Isoprenaline, Levodopa and Carbidopa, Levothyroxine, Lithium, Metaproterenol, Methotrexate, Minoxidil, Phenobarbital, Prazosin, Procainamide, Proxyphylline, Quinidine, Sirolimus, Tacrolimus, Theophylline, Tolazamide, Tolbutamide and Warfarin;

The BE studies should be conducted in accordance with the WHO guidance document, i.e. "Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability", or other international guidelines.

6.3 The original or certified true copies of the electronic documents mentioned in paragraph 6.2.4, 6.2.5 and 6.2.7 above should be submitted to the following address:

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,
Hong Kong (Enquiries: 3974 4175)

If it is necessary to submit the certified true copies of the certificates, please include those pages related to certification in the electronic documents for upload to the PRS 2.0. A certified true copy certifies that the photocopy presented is a true and accurate copy of the original document. Acceptable certification of documents can be done by an independent authority such as Hong Kong solicitor, notary public, the original issuer of the document or Embassy/Consulate.

7. Use of materials of animal origin

7.1 If materials of animal origin are used in the manufacturing of the product, you should also provide documentary evidence obtained from the manufacturer on the source of the animals, the nature of the animal tissues used in the manufacturing and the production processes, showing compliance with one or more of the safety measures taken to minimize the risk of communicable diseases that can be transmitted to human, including but not limited to Transmissible Spongiform Encephalopathy (TSE) transmission promulgated by the European Medicines Agency, USA or Australia. The following documents are relevant:

7.1.1 Notes for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products" released by the European Medicines Agency (EMEA/410/01);

7.1.2 the general monograph of the European Pharmacopoeia on "Products with risk of transmitting agents of animal spongiform encephalopathies";

7.1.3 "Risk and regulatory assessment of lactose and other products prepared using calf rennet" released by the European Medicines Agency;

7.1.4 "Guidance for Industry – the sourcing and processing of gelatin to reduce the potential risk posed by Bovine Spongiform Encephalopathy (BSE) in FDA-regulated products for human use" released by the US-FDA;

7.1.5 Supplementary requirements for therapeutic goods for minimising the risk of transmitting transmissible spongiform encephalopathies (TSEs)" released by the Therapeutic Goods Administration of Australia.

8. General requirements

8.1 Please ensure that all the information set out in paragraph 6 and 7 (if applicable) above have been provided. Additional information may be requested, on a case by case basis, to substantiate the quality, efficacy and safety of the product during evaluation.

8.2 For non-injectable products which differ only in package size, only one application is required for various pack sizes. Separate application of registration is required for the following scenarios:

8.2.1 products with the same description and composition, but different in strengths, e.g. "ABC Tablets 100mg" and "ABC Tablets 50mg";

8.2.2 products presented in different dose forms, e.g. injection, tablet and capsule;

8.2.3 products with more than one presentation for the same pack size;

8.2.4 injectable products with different container volumes, e.g. "ABC Solution for Injection 10mg/5ml" and "ABC Solution for Injection 20mg/10ml".

8.3 For products manufactured by more than one manufacturer, the name, address and role of each manufacturer should be clearly defined. A declaration or flow chart to describe the manufacturing process and the corresponding manufacturer may be required. In general, only one manufacturer will be allowed for each manufacturing step (i.e. single manufacturing pathway). For products with more than one manufacturer involved in one single manufacturing step (i.e. alternative manufacturing pathway), separate application is required for each manufacturing pathway. Please refer to <Supplementary Notes for Application for Registration of Biological Products Involving Alternative / Back Up Manufacturer(s) for Manufacturing Step>.

9. Registration fee

9.1 When an application is approved, you will be required to pay a registration fee of $1,370 per product. You will receive a notification for collection of the Certificate of Drug/Product Registration after the payment. Please pay by post, or via the PRS 2.0 with credit card/PPS

online payment services, or in person by cash or cheque at the address specified in paragraph 6.1 above. Cheque should be made payable to "The Government of the Hong Kong Special Administrative Region" and crossed.

Hours of Shroff office:

Monday to Friday

9:00 am – 1:00 pm and 2:00 pm – 5:30 pm (open until 5:45 pm on Monday)

10. Infringement of patent right

10.1 Please note that the Pharmacy and Poisons Board does not take into consideration of the factor of "patent right" while deciding on an application for registration of a pharmaceutical product/ substance. Nevertheless, an applicant shall not overlook the issue of infringement of patent right. Doing the following acts in Hong Kong without the consent of the patent proprietor may be liable for infringement of a patent registered in Hong Kong:

10.1.1 making, putting on the market, using or importing a patented product; or

10.1.2 stocking the patented product whether for the purpose of putting it on the market (in Hong Kong or elsewhere) or otherwise.

10.2 You are therefore reminded to ensure that your product does not infringe any patent right. Please see sections 73 to 75 of the Patents Ordinance (Cap. 514) for further details. You should always consult your lawyer if you have any doubts on this issue.

11. Enquiries on the progress of applications

11.1 At any stage during the application, you can make enquiry at the Drug Registration Unit regarding the progress of the application. Please quote the file reference of the registration application when making an enquiry.

12. Disclaimers

12.1 These Guidance Notes serve as a general guide to the applicant of new product/ substance registration and shall not be regarded as the complete registration requirements

or authoritative statement of the relevant laws or its interpretation on any particular case. Copies of the Pharmacy and Poisons Ordinance and its subsidiary legislations shall be referred, which can be purchased by calling the Publications Sales Section of Information Services Department at 2537 1910, or by email at puborder@isd.gov.hk. Contents of the relevant legislation can also be found at the Department of Justice's website at https://www.elegislation.gov.hk/.

12.2 These Guidance Notes list out the documents which are generally required to demonstrate the quality, efficacy and safety of the products. Applications for registration of pharmaceutical products may not be accepted if the documents listed in paragraphs 6, 7 and 8 are not submitted via PRS2.0. The Pharmacy and Poisons Board reserves the right to revise these Guidance Notes at any time without giving prior notice. Users are responsible for making their own assessment of these Guidance Notes.