DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION

Guidance Notes on Registration of Pharmaceutical Products/Substances

Preface

This document aims to provide guidance on making application 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);

2. If there is any contradiction between this document and the written laws, the latter shall take precedence. Applicants are strongly encouraged to familiarise themselves with the contents of this guidance notes before submitting their applications.

Pharmaceutical products subject to registration

3. Under the Pharmacy and Poisons Regulations, pharmaceutical products must be registered with the Pharmacy and Poisons Board before they can be sold, offered for sale, distributed or possessed for the purposes of sale, distribution or other use. "Pharmaceutical product" means any substance, or combination of substances:

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

(B) that may be used in, or administered to, human beings or animals, either with a view to –

(i) restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action; or
(ii) making a medical diagnosis.

4. In considering whether or not your product is a “pharmaceutical product”, you should take into account 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 meaning of pharmaceutical product and registration is required. Products commonly referred to as cosmetics, toiletries and disinfectants which do not contain any drug ingredient in its composition and which are sold without any medicinal claims may be excluded. However, it is your obligation to have complete knowledge of the ingredients of products. If the composition of the products for sale is found to contain substances that fall within the meaning of pharmaceutical product, you might commit an offence of the sale of an unregistered pharmaceutical product.

Criteria for registration

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

Who should apply

6. 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.

7. 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.

Pharmaceutical products not subject to registration

8. Products which fall under the following categories are not required to be registered with the Pharmacy and Poisons Board:

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

(B) drug substances imported by licensed manufacturers solely for the purpose of manufacturing their own pharmaceutical products;

(C) products 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;

(D) products imported for re-export only;

(E) products manufactured in Hong Kong for export by the licensed manufacturer only;

(F) products 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.

Where to apply

9. Manual submission of application for registration of pharmaceutical product is no longer accepted with effect from 1 January 2017. You should submit your new application via the online Pharmaceutical Registration System 2.0 (PRS 2.0) at https://www.drugoffice.gov.hk/prs2-ext/client_authentication.jsp

How to apply

10. You should submit the new application via PRS 2.0 together with the following:

(A) the application fee, currently at $1,100 (Please also see paragraph 17 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 Registration and Import/Export Control Division
Drug Office, Department of Health
3/F, Public Health Laboratory Centre,
382 Nam Cheong Street,
Shek Kip Mei, Kowloon,
Hong Kong (Enquiries: 2319 8458)

(B) for products manufactured outside Hong Kong, an authorization letter from the overseas manufacturer for the applicant is required;

(C) the following particulars:

a) soft copy of the business registration certificate of the applicant;

b) an authorized person for the application, contact telephone and facsimile numbers and content of the submission dossier. Please declare in the PRS 2.0 that the applicant "agrees to submit additional or updated supporting documents when required";

c) soft copy and certified true copy (Please see paragraph 10(D) below) of the manufacturer's licence;

d) 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 supply detailed information regarding the manufacturer including the manufacturing and quality control facilities, technical personnel, etc.

e) soft copy and certified true copy (Please see paragraph 10(D) below) of Good Manufacturing Practices (GMP) certificate of the manufacturer. With effect from 1 January 2016, all applications for registration of pharmaceutical products must include evidence of manufacturers' compliance with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP standards. For details, please refer to the "Letter to the Pharmaceutical Trade" and "Questions and Answers on PIC/S GMP Requirements for Registration of Pharmaceutical Products" available at http://www.drugoffice.gov.hk;

f) soft copy and original or certified true copy (Please see paragraph 10(D) below) of free sale certificate of the product issued by the country of origin;

g) one set of prototype sales pack (e.g. outer carton, container label, and other component(s) comprising the sales pack) for each pack size of the product, complying with the labelling requirements. Please refer to the "Guidelines on the Labelling of Pharmaceutical Products" at **Appendix 2**;

h) for products containing a new chemical or biological entity:

(i) official evidence of registration approval of the product (e.g. soft copy and original or certified true copies (Please see paragraph 10(D) below) of free sale certificates) in two or more 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. (Please see Note (1) below);

(ii) expert evaluation reports on the safety, efficacy and quality of the product. Curriculum vitae of the expert and the expert's signature on the corresponding reports are required;

(iii) European Union Risk Management Plan (EU-RMP) and/or US Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategy (REMS) are required for the product, if applicable. Information on whether any of the risk management plan activities and mitigation strategies will be implemented in Hong Kong;

(iv) proposed package insert of the product. Where the package insert is in the form of a patient information leaflet, a prescribing information leaflet for healthcare professionals for use in Hong Kong should also be submitted;

Note (1): In the case of applications for registration of new chemical or biological entity that cannot provide the official evidence of registration approval in two or more of the listed

countries in paragraph 10(C) h) (i) but

- there is a local unmet medical need of the product for communicable diseases or matters of public health importance in the areas of tuberculosis, emerging and/or re-emerging infectious diseases (e.g. avian influenza, chicken pox, Ebola, etc.) and antimicrobial resistance; and
- the product for the communicable diseases or matters of public health importance is promulgated by reputable international health agencies on human or veterinary medicines, including the World Health Organization (WHO), World Organisation for Animal Health, etc.;

the applications may also be accepted for evaluation on a case by case basis. The applicants are additionally required to provide the following:

- justification for non-compliance to paragraph 10(C) h) (i) above; and
- an assessment report on safety and efficacy of the product to be prepared by a local expert with fellowship or equivalent qualification and he/she has at least 5 years of experience in the field relevant to the product.

i) clinical and scientific documentation substantiating the safety and efficacy of the product:

(i) except for generic product applications received on or after 1 October 2012 and their originator products have been registered in Hong Kong for over 8 years (please see paragraph 10(C) j) below);

(ii) for biosimilar product applications, please also refer to the "Guidance Notes for Registration of Biosimilar Products" available at the website http://www.drugoffice.gov.hk/eps/do/en/doc/guidelines_forms/Biosimilar_guidelines_revised_Final_ENG.pdf?v=tmg955a;

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

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

(ii) documentary evidence showing that the package insert has been approved by one of the listed countries in paragraph 10(C) h) (i) above;

k) (i) in the case of applications for registration of pharmaceutical substances:
Sample of the pharmaceutical substance as it will be sold to the purchaser. For imported substance, you are reminded to apply for an import licence before importing the samples. Please refer to the attached "How to apply for Import and Export Licences for Pharmaceutical Products and Medicines", "How to complete Import and Export Licence forms for Pharmaceutical Products and Medicines" and "Import and Export Licences Notes for the Guidance of Applicants" at **Appendix 4** for details.

OR

(ii) in the case of applications for registration of pharmaceutical products:
Scanned image in Portable Document Format (PDF) format (scanning based on 300dpi or higher) or photograph image in JPEG format (pixel size not less than 320x200) of your prototype sales pack or sample sales pack, including the 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 example:

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

l) detailed and complete qualitative and quantitative composition of the finished product issued by the manufacturer. Batch formula is not accepted as alternative to the requirement. Non-proprietary names of ingredients, colour index number or E-number for all colourants used (including capsule shells) should be provided. (Please see Note (2) below);

m) specifications of the product issued by the manufacturer. Document(s) showing compliance with one or more of the following pharmacopoeias 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 also refer to paragraph 13 for products containing vitamins, minerals, etc. (Please see Note (2) below);

Note (2): Please refer to the "General Requirements for Master Formula and Specifications for Non-Biological Products" at **Appendix 1**

n) detailed method of analysis of the product for all tests stated in the finished product specifications. Please also refer to paragraph 13 below for products containing vitamins, minerals, etc.;

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

p) stability test data of the product at one of the following

temperature(˚C)/ relative humidity (RH) conditions:

Real Time Testing Condition

(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 Condition

(iv) 40˚C+/-2˚C/75%+/-5% RH for 6 months*

*At least 3 months' real-time stability test data must be available at the time of submission of applications on or after 1 April 2011.

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.

q) Bioequivalence (BE) data:

(i) 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.

(ii) for critical dose drugs/ narrow therapeutic range drugs (with effect from 1 August 2016) 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.

(D) Soft copies of the above supporting documents must be submitted via the PRS 2.0 in PDF format. The original or certified true copies of the above supporting documents should be submitted to the following address:

Drug Registration and Import/Export Control Division
Drug Office, Department of Health
3/F, Public Health Laboratory Centre,
382 Nam Cheong Street,
Shek Kip Mei, Kowloon,
Hong Kong (Enquiries: 2319 8458)

Imposing sales control on new chemical or biological entity

11. In general, when an application for registration of a pharmaceutical product containing new chemical or biological entity (NC/BE) is approved by the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee, the product can be registered once appropriate sales control has been imposed by the enactment of legislative amendment to the Pharmacy and Poisons Regulations. The certificate of registration will then be issued subject to payment of registration fee.

12. To facilitate timely registration of pharmaceutical product containing NC/BE, the Pharmacy and Poisons Board determined that with effect from June 2018, once an application of the concerned product is submitted and accepted for evaluation, or is listed in public medical assistance programme, the legislative amendment procedures to impose appropriate sales control would be commenced unless it is necessary to seek advice (e.g. if the sale control is subjected to the indications or dosage of the product to be approved) from the Pharmacy and Poisons (Registration of Pharmaceutical Products

and Substances: Certification of Clinical Trial/Medicinal Test) Committee in advance.

Registration of products containing vitamins, minerals, etc.

13. Special exemptions are provided for the quality analysis of products containing vitamins, minerals, etc. Please refer to the "Guidelines on the Testing of Pharmaceutical Products containing Vitamins, Minerals, etc." at **Appendix 3** for details.

Use of materials of animal origin

14. 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:

(A) "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);

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

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

(D) "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 FDA;

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

General Requirements

15. Please ensure that all the information set out in paragraph 10 (C) above have been provided.

16. For products of the same description, composition and strength but different package sizes, only one application is required. For instance, only one application is required for "ABC Tablet 100mg" of package sizes 10's, 100's and 1,000's. However, two separate applications are required for "ABC Tablet 100mg" and "ABC Tablet 50mg". Similarly, separate applications are required for a product presented in different dose forms, e.g. injection, tablet and capsule. One presentation is allowed for each pack size and you should submit two separate applications for registration if you intend to market the product in two different presentations for the same pack size.

Registration fee

17. When an application is approved, you will be required to pay a registration fee of $1,370 per product. You will receive the Certificate of Drug/Product Registration when we have received the payment. Please pay by post, or via the PRS 2.0 with credit card/PPS online payment services, or in person at the address specified in paragraph 10(A) above. Cheques 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)

Infringement of patent right

18. 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 as 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:

(A) making, putting on the market, using or importing a patented product; or

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

19. 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.

Enquiries on progress of applications

20. At any time 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 enquiry.

21. The Guidance Notes are served 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/.