INFORMATION NOTE

Registration of proprietary Chinese medicines in Macao, Taiwan and the Mainland

1. Background

1.1 At its meeting held on 17 January 2011, the Panel on Health Services requested the Research Division to provide information on the registration of proprietary Chinese medicines ("pCms") in Macao, Taiwan and the Mainland, particularly relating to how these places address major concerns raised at the meeting. Such concerns broadly cover the following areas:

(a) registration requirements for pCms;

(b) regulatory bodies and their composition (if applicable);

(c) evaluation criteria used in the technical review of pCms and relevant timelines; and

(d) transparency of the registration process.

1.2 Among the selected places studied, only Taiwan and the Mainland have in place a registration system for pCms, while Macao has not implemented such a registration system[1]. Registration for pCms in both Taiwan and the Mainland is regulated by registration requirements applicable to traditional Chinese medicines in general, and there are no separate regulations governing pCms registration in both places.

1.3 The key features of the registration mechanism for pCms in the selected places are summarized in the **Appendix**.

[1] 澳門衞生局 (2010).

2. Regulation of proprietary Chinese medicines in Macao

Relevant legislation

2.1 In Macao, there is no legal definition for pCm. *Decreta-Lei n 53/94/M* ("53/94/M"), enacted in 1994, is the main legislation governing the licensing and operating conditions of import, export and wholesale companies and pharmacies of traditional Chinese medicines. According to 53/94/M, traditional Chinese medicines refer to any medicines or any plant or animal ingredients or any materials extracted from these ingredients that are used according to traditional Chinese medicine and Chinese pharmacology for the prevention or treatment of diseases, or the regulation of bodily functions. (Article 1)

Regulatory measures of proprietary Chinese medicines

2.2 In Macao, each lot of locally produced and imported pCm has to obtain pre-approval from the Health Bureau of the Macao Special Administrative Region Government ("the Health Bureau") before sale with the submission of dossiers of safety information, including microbiological limits, heavy metals and toxic element content. For pCms containing materials from cattle, the applicant has to provide the source of the cattle-derived ingredients and the drug GMP ("good manufacturing practice") certificate awarded to the manufacturer.[2] In addition, the Macao government bans the manufacture, import and sale of Aristolochiaceae plants and their preparations.[3]

2.3 While Macao does not have a registration system for pCms, it implements an "alternative registration system", under which pCms and other traditional Chinese medicines from a country with a registration system in place may be exempted from submitting test reports of microbiological limits, heavy metals and toxic element content, with the presentation of the certificate of free sale or certificate of registration of the country of origin or exporting country/region.

[2] Chief Executive's Decision No. 120/2005.

[3] 澳門衞生局藥物事務廳藥物監測暨管理處 (2006).

2.4 Other regulatory measures for traditional Chinese medicines adopted in Macao include:[4]

(a) announcing a "List of Traditional Chinese Medicine Ingredients applied in the Macao Special Administrative Region" by the Health Bureau, which consists of three sub-lists:

(i) Part I: toxic traditional Chinese materials (30 types);

(ii) Part II: common therapeutic traditional Chinese materials (562 types); and

(iii) Part III: Chinese medicinal materials that are also used as food (112 types); where all traditional Chinese materials under Parts I and II are restricted for sale by licensed Chinese pharmacies;

(b) providing the public with the necessary instructions regarding the use and side effects of drugs, particularly for those toxic drugs (Article 15(3c) of 53/94/M); and

(c) where necessary, in order to safeguard consumer health, the Director of the Health Bureau issuing instructions to the responsible persons of establishments of traditional Chinese medicines and prohibiting the manufacture and supply of products that have been proven to be harmful to health.

2.5 Under Article 18(4) of 53/94/M, the production and sale of products in violation of the law are subject to seizure. Breaches of the rules governing the import and export of traditional Chinese medicines are subject to a fine of up to MOP$100,000 (HK$97,000)[5] with the products concerned to be forfeited.[6]

[4] 澳門衞生局藥物事務廳藥物監測暨管理處 (2006).

[5] The average exchange rate in January 2011 was MOP$1= HK$0.97.

[6] Article 36, *Foreign Trade Act*.

2.6 Article 22 of 53/94/M allows that decisions taken by the Director of the Health Bureau be appealed to the Administrative Court of Macao.

Statutory body relating to the regulation of traditional Chinese medicines

2.7 A statutory body accountable to the Director of the Health Bureau, the Technical Committee on Affairs of Traditional Chinese Pharmacy (中藥事務技術委員會), has been established under Article 23 of 53/94/M with the following terms of reference:

(a) providing opinions on the licensing of establishments engaged in the preparation and marketing of products of traditional Chinese medicines, and on the list of materials that is available only at traditional Chinese pharmacies as well as the list of toxic medicines that is available only by prescription;

(b) conducting research and proposing necessary measures to promote the practice of traditional Chinese medicine and traditional Chinese medicine businesses on the basis of scientific and technical knowledge;

(c) proposing guidelines to improve the operation of establishments engaged in the preparation and marketing of products of traditional Chinese medicines; and

(d) advising on matters relating to traditional Chinese medicine that are submitted to the Director of the Health Bureau.

2.8 This Committee comprises the following members:

(a) Director of the Department of Pharmaceutical Affairs (藥物事務廳廳長);

(b) two technicians with knowledge in traditional Chinese medicine; and

(c) two representatives from the Macao Association of Traditional Chinese Medicine (澳門中藥業公會).

Latest developments

2.9 According to the Health Bureau[7], draft administrative regulations for the implementation of registration requirements for pCms have been prepared by the Health Bureau at the end of 2010, and the relevant legislative process is about to commence. These administrative regulations establish standards for quality, safety and efficacy of pCms, and specify requirements for package labelling and inserts of these products.

3. Registration of proprietary Chinese medicines in Taiwan

Definition of proprietary Chinese medicines

3.1 Under the *Pharmaceutical Affairs Act* (Article 10), medicines which are prepared in accordance with traditional Chinese prescriptions and have therapeutic efficacy are referred to as "preparations of inherited formulation" (固有成方製劑).[8] In general, any form of Chinese herbal medicines that claims to have therapeutic effects is regulated as medicines under the *Act*.

Relevant legislation

3.2 In Taiwan, the main legislation for drugs and medical devices is the *Pharmaceutical Affairs Act*, which was adopted in 1970 and revised in 2006. Regulations relating to the registration of drugs are set out in the *Provisions Governing the Examination and Registration for Drugs* (《藥品查驗登記審查準則》), which was established in 2005 in accordance with Article 39 of the *Pharmaceutical Affairs Act.* These Provisions also cover requirements relating to the post-approval change, transfer, extension and reissue of drug licences. As regards registration of traditional Chinese medicines, specific guidelines on relevant matters have been developed, including *Guidelines on Examination and Registration of Domestic Traditional Chinese Medicines* and *Guideline on Examination and Registration of New Chinese Medicines.*

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7 澳門衞生局 (2010).

8 Preparations refer to medicines which are processed and compounded from therapeutic raw materials into a specific pharmaceutical form and dosage. Preparations of inherited formulation are classified into medicines prescribed by Chinese medicine practitioners, over-the-counter drugs, and single herb for dispensation of drugs. See 劉尚志 (2005)，第 200 頁 .

Reference standards

3.3 According to Article 74 of the *Provisions Governing the Examination and Registration for Drugs*, the testing specifications for traditional Chinese medicines should follow those mentioned in the "Taiwan Herbal Pharmacopoeia" (《台灣傳統藥典》) or other foreign pharmacopoeias or announcements acknowledged by the Department of Health, Executive Yuan ("DOH"). It is required that references can only be taken from the latest two editions.

Regulatory authorities

3.4 The Committee on Chinese Medicine and Pharmacy ("CCMP") of DOH is the regulatory authority at the central level handling matters concerning the registration of traditional Chinese medicines, whereas municipal and county/city governments act as the competent authorities at the local level.

Committee on Chinese Medicine and Pharmacy

3.5 Established under DOH in 1995 by law, CCMP is composed of four divisions, namely Division of Chinese Medicine, Division of Chinese Pharmacy, Division of Research and Development and Division of Information and Publications, and a Technology Policy Unit. These divisions/unit handle matters concerning the administration affairs (including registrations of traditional Chinese medicines, and changes and extension of relevant drug licences), research and development, and digitalization of classic literature on Chinese medicine and pharmacy respectively.

3.6 CCMP comprises a chairperson and 15 members. Most of them are university professors and chairpersons of professional associations on traditional Chinese medicine and pharmacy.

Other government organizations related to registration of proprietary Chinese medicines

3.7 Two divisions of the Taiwan Food and Drug Administration ("TFDA"), a subsidiary of DOH, also assist in the registration of pCms:

(a) Division of Research and Analysis, with its Section of Chinese Medicine Analysis being responsible for conducting the review and inspection for registration of traditional Chinese medicines; and

(b) Division of Drugs and New Biotechnology Products, with its Section of New Drugs being responsible for evaluating and regulating new drugs (including traditional Chinese medicines) and imported active pharmaceutical ingredients applying for registration.

Registration requirements

3.8 Under the *Pharmaceutical Affairs Act*, the manufacturing and importation of drugs (including traditional Chinese medicines) in Taiwan is subject to registration and market approval by DOH, with which the necessary information on the drug (including the ingredients, specifications, functions, summary of the manufacturing process, specifications and methods of testing and related certificates, together with the fee paid) is filed (Article 39). No manufacturing or importation of such drugs shall be allowed until a drug licence is approved and issued.

Registration categories

3.9 In Taiwan, Chinese medicines may be registered under three registration categories:

(a) domestic traditional Chinese medicines;

(b) imported traditional Chinese medicine products; and

(c) new Chinese medicines, including traditional Chinese medicines with new therapeutic efficacy, new route of administration and new compound preparations.

General requirements for the applicant

3.10 The general requirements for an applicant applying for registration of traditional Chinese medicines include:

(a) for registration of domestic traditional Chinese medicines, being a company with a pharmaceutical business permit, a plant registration permit (exempt for importing medicines), and corporate registration (for a corporate organization) or for-profit business registration (for a non-corporate organization); and

(b) for registration of imported traditional Chinese medicines, being a company with a manufacturing permit or a certificate of free sale issued by the country of production.

Information requirements for application

3.11 The application for registration of traditional Chinese medicines should be submitted to DOH. Documents and other materials required in the application dossier are:

(a) a completed form for application for registration of the Chinese medicine products;

(b) entrustment papers submitted by the manufacturing factory or its parent company, together with the name, type, ingredient content (raw materials should be expressed using the Chinese medicine names) and quantity of the drug;

(c) outer boxes, package inserts and labels to be used for the drug;

(d) photocopy of the formulation basis;

(e) documentation of operational procedures and reports of stability studies;

(f) inspection specifications and methods (in Chinese or English) for all prescription ingredients (including supplementary raw materials and colour agents added during manufacture), in compliance with those announced by DOH;

(g) all inspection results for the ingredients and raw materials in the prescription (including supplementary additives during manufacture); and

(h) for imported products, relevant licences and certificates, batch records, and documental proof of authorization for manufacture.

(A) Data exemption

3.11.1 Under Article 92 of the *Provisions Governing the Examination and Registration for Drugs*, an applicant may be granted exemption from the requirements of using the High Performance Liquid Chromatography (HPLC) method for analysis of the traditional Chinese medicine for formulas not covered in well-established publications acknowledged by DOH, provided that this is deemed to be difficult to implement by DOH.

(B) Protection of data

3.11.2 It is required that trade secrets of the drug manufacturers provided in the applications for the manufacturing and importation of drugs be kept in confidence by the relevant authorities (Article 40-1 of the *Pharmaceutical Affairs Act*). However, such requirement is not applicable to information concerning drug ingredients, package inserts, summary of the clinical trial protocol and drug safety.

Fee requirements

3.12 In Taiwan, standard fees are collected for registration of traditional Chinese medicines. The following standard fee schedule has been set up by DOH:[9]

(a) registration of traditional Chinese medicine preparations:

(i) evaluation fee: NT$4,000 (HK$1,104);

(ii) issuance of licence: NT$1,000 (HK$276); and

[9] 行政院衞生署 (2009).

(iii) factory inspection: NT$10,000 (HK$2,760) (newly established plant in Taiwan) or NT$20,000 (HK$5,520) (overseas plant); and

(b) registration of new traditional Chinese medicine preparations: NT$41,000 (HK$11,316) in total.[10]

Penalties

3.13 Any person manufacturing or importing a drug without being approved and issued a drug licence will be imposed a fine of not less than NT$30,000 (HK$8,280) but not more than NT$150,000 (HK$41,400). (Article 92 of the *Pharmaceutical Affairs Act*)

Review and approval process

3.14 The review and approval process for registration of traditional Chinese medicines commences upon the applicant's submission of the full application dossier to DOH. Such process involves several major steps, including:

(a) assessment of the submitted materials, and site inspection on the quality control, production records, manufacturing process and on-site supervision situation by TFDA. The purpose of site inspection is to ascertain that the plant has the actual production capacity;

(b) review by CCMP on aspects regarding the prescription, the pharmaceutical plant or business and the manufacturing process so that it could make approval decision of the registration application based on the review results;

(c) arrangement to conduct clinical trial of samples by the applicant within the specified time, upon receiving notice of registration acceptance from CCMP. The clinical trial should be conducted in Taiwan in accordance with publicized requirements;

(d) assessment and approval of results of the clinical trial by TFDA; and

[10] The average exchange rate in January 2011 was NT$1= HK$0.276.

(e) issuance of drug licence by CCMP. It is noted that a drug licence for a domestic traditional Chinese medicine may be issued to the applicant to commence production or marketing of the drug before the clinical trial is carried out. Based on TDFA's assessment of the results of the clinical trial, only a qualified drug is allowed to continue to be manufactured or marketed. On the other hand, the issued licence of a disqualified drug will be cancelled, and a public announcement about the cancellation will be made.

Timelines

3.15 The *Provisions Governing the Examination and Registration for Drugs* specify the following timelines for the applicant:

(a) collection of the drug licence after receiving notice: three months, otherwise, the drug licence may be cancelled; and

(b) sending testing samples for clinical trial after receiving a drug testing notice: 30 days (domestic traditional Chinese medicines) or three months (imported traditional Chinese medicines), otherwise, the application may be considered withdrawn.

Appeal mechanism against registration decision

3.16 An applicant may appeal with sufficient reason in writing, together with attachments of literature references and relevant documents, to CCMP within two months after receiving notice of the decision. Only one application for re-examination is allowed.

Measures for increasing the openness and transparency of the registration process

3.17 In Taiwan, measures are adopted by the regulatory authorities to provide the public and particularly the industry with more information on the registration application process of traditional Chinese medicines, hence enhancing their understanding of relevant issues. Some of these measures include:

(a) for the purpose of protecting public interests, DOH publicizing the data submitted for drug examination and registration through different methods, such as government gazette or other publications, some telecommunication means and Internet;

(b) organizing educational seminars by CCMP to promote the laws and regulations concerning traditional Chinese medicines among industry stakeholders (one to three times annually);

(c) collecting views by establishing communication platforms with industry stakeholders by holding regular working meetings together with DOH and other related Ministries; and

(d) answering questions on matters relating to registration of traditional Chinese medicines on the Websites of both the central and local authorities.

4. Registration of proprietary Chinese medicines in the Mainland

Definition of proprietary Chinese medicines

4.1 There is no legal definition of pCm in the Mainland. According to the State Food and Drug Administration ("SFDA"), pCms (also known as Chinese patent medicines) refer, in a broad sense, to any processed products of Chinese herbal medicines, including but not limited to ready-made medicines in different forms prepared on the basis of certain therapeutic principles, such as pills, powder and granules.[11] In the Mainland, traditional Chinese medicines cover both medicinal materials and their preparations based on the traditional Chinese medicine theories.[12]

[11] 國家食品藥品監督管理局 (2006).

[12] Zhang, W (2008).

Relevant legislation

4.2 In the Mainland, traditional Chinese medicines are governed by requirements laid down in the following laws and regulations:

(a) *Drug Administration Law*, adopted in 1984 and revised in 2001, having the goals of protecting the public health and promoting economic development in the pharmaceutical sector by stipulating the responsibilities and obligations of drug manufacturers, distributors, and institutions that provide services to the drug industry;

(b) *Provisions for Drug Registration*, adopted in 1985 in accordance with the *Drug Administration Law*, governing the process of application, review and approval of drug registration. The latest revision came into effect in October 2007; and

(c) *Supplementary Rules for Traditional Chinese Medicine Registration*, implemented in July 2008, specifying supplementary requirements for the registration of traditional Chinese medicines.

Reference standards

4.3 The Mainland has established a national drug standard system based on two components:

(a) the Pharmacopoeia of the People's Republic of China (《中國藥典》), which is a code for drug quality control, safety and efficacy. Standards relating to pCms are included in Volume I of the Pharmacopoeia; and

(b) specifications set by SFDA or other bureaux (部局頒標準).

4.4 These drug standards are compulsorily applied nationwide and must be strictly observed in drug research, production, distribution, administration and management. Enterprises are encouraged to formulate and apply registration standards higher than the national standards.

4.5 The latest edition of the Pharmacopoeia (2010) contains 1 063 kinds of pCms, whereas standards made by SFDA cover 4 690 pCms.

Regulatory authorities

4.6 SFDA is the central regulatory authority in charge of drug registration nationwide, administrative supervision and technical supervision regarding the research, production, distribution, and use of drugs (including traditional Chinese medicines and their preparations) and medical devices. Drug regulatory departments of the provinces, municipalities and counties directly under the Central Government act as the local regulatory authorities. At the end of 2007, there were 2 692 local drug regulatory departments in the Mainland, including 31 at the provincial level, 339 at the municipal level and 2 321 at the county level.[13]

Other government organizations related to registration of proprietary Chinese medicines

4.7 Several subsidiaries of SFDA are involved in the registration of pCms, and they are:

(a) Department of Drug Registration ("DDR"), being the key organization taking charge of drug registration. DDR is also responsible for, among others, developing the standard practices of traditional Chinese medicine preparation and implementing the protection system for traditional Chinese medicines;

(b) Centre for Drug Evaluation ("CDE"), assisting in the drug registration work by conducting scientific review of new drugs, imported drugs, generic drugs, and over-the-counter medications;

(c) National Institute for the Control of Pharmaceutical and Biological Products ("NICPBP"), being responsible for registration testing of pharmaceutical products, biological products and medical devices, and verification of registration specifications of these products, as well as providing verification opinions; and

[13] The Information Office of the State Council (2008).

(d) Chinese Pharmacopoeia Commission, being a technical organization responsible for setting and revising national drug standards.

Registration requirements

4.8 Under Article 3 of the *Provisions for Drug Registration*, drug registration refers to the process of review and approval in which SFDA evaluates the safety, efficacy and quality of the drugs applied for marketing, and decides whether or not to approve such an application. Only those drugs that have been issued a drug approval number or an import drug licence are allowed to be produced or sold in the Mainland, with the exception of some traditional Chinese medicines and the prepared slices of traditional Chinese medicines (中藥飲片) on which such a requirement has not been imposed.[14]

Registration categories

4.9 According to *Annex 1: Registration Categories and Application Dossier Requirements for Traditional Chinese Medicines and Natural Medicinal Product* of the *Provisions for Drug Registration*, traditional Chinese medicines may be registered under nine registration categories:

(a) active ingredients extracted from plants, animals and minerals and their preparations, not yet marketed in the Mainland;

(b) newly discovered traditional Chinese medicines and their preparations;

(c) substitutes of traditional Chinese medicines;

(d) new medicinal parts of traditional Chinese medicines and their preparations;

[14] According to Article 31 of the *Drug Administration Law*, a gradual implementation of the requirement to obtain approval number for traditional Chinese medicines and the prepared slices of traditional Chinese medicines shall be adopted. Nevertheless, a timeframe for full implementation of such requirement has not been announced. See 醫藥經濟報 (2010).

(e) active fractions extracted from plants, animals and minerals and their preparations, not yet marketed in the Mainland;

(f) compound preparations made from traditional Chinese medicines or natural drugs, not yet marketed in the Mainland;

(g) preparations made from traditional Chinese medicines or natural drugs with changed route of administration, already marketed in the Mainland;

(h) preparations made from traditional Chinese medicines or natural drugs with changed dosage form, already marketed in the Mainland; and

(i) traditional Chinese medicines or natural drugs following the national standard.

4.10 Categories (a) to (h) above are subject to regulatory review for new drug registration, whereas category (i) subject to regulatory review for drugs following existing national standard that have been approved to be marketed by SFDA (generic drug registration).

General requirements for the applicant

4.11 The following general requirements are imposed on an applicant applying for registration of traditional Chinese medicines:

(a) a domestic applicant shall be an institution legally registered within the People's Republic of China that independently assumes civil liability; and

(b) an overseas applicant shall be a legal overseas drug manufacturer, or for an overseas applicant for import drug registration, its branch or entrusted agency shall be within the People's Republic of China.

Information requirements for application

4.12 An applicant applying for registration of traditional Chinese medicines should complete the "Application Form for Drug Registration" and submit it together with the necessary materials to the relevant local drug regulatory department (or SFDA directly for imported drugs), which checks that the dossier content and format of the submitted materials are in line with the requirements. Article 49 of the *Provisions for Drug Registration* states that the application dossier can only be submitted once, and applicants may not supplement technical data on their own during the application process. Generally speaking, four sets of information are required in the application dossier:

(a) general information, such as name of the drug, conclusions and evaluations of the results of pivotal studies, specimen of the proposed labelling and packaging to be used;

(b) files of pharmaceutical research, such as origin and identification of Chinese materia medica, technology for cultivation, processing and production, and relevant studies and literature, proposed quality standard and results and relevant literature on stability studies;

(c) files of pharmacological and toxicological research, such as relevant literature on pharmacodynamics tests, acute and long-term toxic studies, allergy tests, haemolytic tests and cancer causing test; and

(d) files of clinical research, such as protocols for clinical trials, manual for clinical investigators, ethics committee approval and clinical test reports.

4.13 A drug being applied for importation should have obtained marketing authorization in the country or region of production, with proofs of compliance with the GMP requirements of the country or region of production and the Mainland. Alternatively, those overseas manufacturers without drug marketing authorization in the country or region of production may submit application documents to SFDA along with reports of clinical studies conducted in the Mainland, confirming that the drug meets the safety, efficacy and clinical standards required by SFDA.

(A) Data exemption

4.13.1 According to DDR, the data required for registration applications of preparations based on famous classical herbal formula may be partially exempted on account of their history of clinical treatment, sources of formula, functions and indications, and manufacturing procedures.[15] Further, traditional Chinese medicines and their preparations not previously marketed in the Mainland may be entitled to a "fast-track" special review and approval procedure, subject to CDE's discretion (Article 45 of the *Provisions for Drug Registration*).

(B) Protection of data

4.13.2 It is stipulated in the *Provisions for Drug Registration* that the drug regulatory departments, relevant institutions and persons involved in drug registration have to keep the technical secrets and trial data submitted by the applicant in confidence. (Article 9) Specifically for drugs containing new chemical entities, if the drug regulatory department and its staff members release undisclosed experimental data or other materials submitted by an applicant obtaining approval of production or marketing of those drugs, and hence causing losses to the applicant, the drug regulatory department may be liable for compensation. (Article 72 of the *Regulations for Implementation of the Drug Administration Law*)

Fee requirements

4.14 Drug regulatory departments are allowed to collect fees for drug registration, drug certification, drug testing for approval and mandatory drug testing, as set out in the *Regulations for Implementation of the Drug Administration Law.*

[15] Zhang, W. (2008).

Penalties

4.15 There are no specified penalties for selling, producing or possessing traditional Chinese medicines or their preparations without an approval number or import drug licence. However, Article 74 of the amended *Drug Administration Law* states that if counterfeit drugs are produced or sold, the drugs illegally produced or sold and the illegal gains shall be confiscated, and a fine not less than two times but not more than five times the value of the drugs concerned shall be imposed. Any approval documents granted may be withdrawn and an order may be given to suspend production or business operation for rectification. In serious cases, the certificate for manufacture, supply or distribution of the drugs may be revoked, and the parties concerned may be subject to criminal investigation.

Review and approval process

4.16 Similar to Taiwan, the review and approval process for registration of traditional Chinese medicines in the Mainland involve several major steps:[16]

(a) on-site inspection conducted by the relevant drug regulatory department on the research and development conditions and raw data of the drug after preliminary review of the submitted documentations;

(b) delivery of review opinions, inspection reports and the application dossier by the drug regulatory department to CDE, which organizes pharmaceutical, medical and technical personnel to conduct technical review of the submitted dossier on aspects of safety, efficacy and quality of the drug;

(c) testing of samples according to the specifications submitted by the applicant and verification of specifications[17] by an authorized or designated drug testing institute (such as NICPBP for imported drugs);

(d) on-site inspection of the production site by CDE to verify the applicability of the manufacturing processes and conduct sample collection;

[16] Zhang, W. (2008).

[17] Specification verification includes laboratory testing and review on the feasibility and scientific basis of the testing methods and the controllability of the proposed indicators of drug quality.

(e) CDE making general opinion based on the technical review, site inspection reports and sample testing results, and reporting the general opinion together with relevant documents to SFDA; and

(f) SFDA making approval decision based on CDE's general opinion.

Timelines

4.17 Chapter XII of the *Provisions for Drug Registration* specifies the following timelines for various steps of the registration process:

(a) acceptance of application and preliminary review by local drug regulatory departments: five days;

(b) completion of work by local drug regulatory departments[18]: 30 days from the date an application is accepted;

(c) sample testing and specifications verification by a drug testing institute: 60 days (90 days for controlled drugs and vaccine);

(d) technical review by CDE:

(i) new drug application for production: 150 days;

(ii) the application for changing the dosage form of a marketed drug or for a generic drug: 160 days; and

(e) making review and approval decision by SFDA: 20 days, plus an extension of 10 days subject to approval of the Head of SFDA.

[18] The relevant work covers: checking drug development conditions and raw data; reviewing application dossiers; sampling; notifying drug testing institutes for conducting testing for drug registration; submitting the review opinions, inspection report and application dossiers to SFDA; and notifying the applicant of the review opinions.

Appeal mechanism against registration decision

4.18 SFDA has a system of appeal in place to handle complaints against any decision made in relation to drug registration. Under the system, an applicant may submit a completed "Application Form for Drug Registration Second Review" to SFDA with reasons provided within 60 days after receiving the decision. SFDA will make a second review decision, and notify the applicant its decision within 50 days after receiving an application for second review. If the original decision is affirmed, SFDA will not accept any further application for second review thereof.

Measures for increasing the openness and transparency of the registration process

4.19 In order to increase the level of openness and transparency in the technical evaluation for drug registration, SFDA and local drug regulatory departments have adopted the following measures:[19]

(a) providing applicants with comprehensive information on the application process (on official websites or at official premises), including application procedures, application charges, timelines, required application materials and lists of officials in charge of the application, inspection, review and approval;

(b) providing applicants with access to information on the status of the acceptance, examination, inspection, review and approval of drug registration application and the final resolution;

(c) making non-acceptance or disapproval decision to the applicant in writing with reasons;

(d) officials with a possible interest in the applicant or application not being involved in the approval process;

(e) conducting public hearings for matters of public interests or deemed to be of vital importance to the public before making administrative decisions;

[19] Zhang, W. (2010).

(f) enhancing communication and exchange with applicants in the forms of expert consultation meetings, voluntary consultation meetings, video conferences, and teleconferences; and

(g) where appropriate, disclosing cases of evaluation on the Website of the drug regulatory departments.

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Appendix

Key features of registration mechanism for proprietary Chinese medicines in Macao, Taiwan and the Mainland

	Macao	Taiwan	The Mainland
Regulatory framework for registration of proprietary Chinese medicines			
Legal definition of proprietary Chinese medicine (pCm)	Nil.	Under the *Pharmaceutical Affairs Act* (Article 10), medicines prepared in accordance with traditional Chinese prescriptions and having therapeutic efficacy are referred to as "preparations of inherited formulation" (固有成方製劑).	Nil. According to the State Food and Drug Administration (SFDA), pCms refer, in a broad sense, to any processed products of Chinese herbal medicines, covering the ready-made medicines in different forms prepared on the basis of certain therapeutic principles.
Availability of a registration system for pCms	No.(1)	Yes.	Yes.
Relevant legislation	Not applicable.	Regulation of pCm registration covered under legislation for medicines in general: (a) *Pharmaceutical Affairs Act*; and (b) *Provisions Governing the Registration and Market Approval of Drugs*.	Regulation of pCm registration covered under legislation for medicines or Chinese medicines in general: (a) *Drug Administration Law*; (b) *Provisions for Drug Registration*; and (c) *Supplementary Rules for Traditional Chinese Medicine Registration*.

Note: (1) Macao implements an "alternative registration system", under which pCms from a country with a registration system in place may be exempted from submitting test reports, with the presentation of the certificate of free sale or certificate of registration of the country of origin or exporting country/region.

Appendix (cont'd)

Key features of registration mechanism for proprietary Chinese medicines in Macao, Taiwan and the Mainland

	Macao	Taiwan	The Mainland
Regulatory framework for registration of proprietary Chinese medicines (cont'd)			
Reference standards for pCms	Not specified.	(a) "Taiwan Herbal Pharmacopoeia" (《台灣傳統藥典》); and (b) foreign pharmacopoeias or announcements acknowledged by the Department of Health, Executive Yuan (DOH).	(a) Pharmacopoeia of the People's Republic of China (《中國藥典》); and (b) specifications set by SFDA.
Major authority for pCm registration	Not applicable.	Committee on Chinese Medicine and Pharmacy (CCMP) of DOH. CCMP comprises a chairman and 15 members, most of them being university professors and chairmen of professional associations in traditional Chinese medicine and pharmacy.	SFDA, with its Department of Drug Registration being the key organization in charge of drug registration.

Appendix (cont'd)

Key features of registration mechanism for proprietary Chinese medicines in Macao, Taiwan and the Mainland

	Macao	Taiwan	The Mainland
Registration process of proprietary Chinese medicines			
Technical evaluation procedures taken by the regulatory authorities	Not applicable.	(a) site inspection; (b) review on the prescription, the pharmaceutical plant or business, and the manufacturing process; (c) conduct of clinical trial of samples (arranged by the applicant); and (d) assessment and approval of results of the clinical trial.	(a) on-site inspection by local drug regulatory authorities; (b) technical review of the submitted dossier on aspects of safety, efficacy and quality of the drug; (c) testing of samples and verification of specifications; and (d) on-site inspection of the production site by the central regulatory authority for verification of the applicability of the manufacturing processes.
Timelines for registration approval	Not applicable.	Specified for the applicant: (a) collection of the drug licence after receiving notice: three months (uncollected licence may be cancelled); and (b) conducting sample testing after receiving a drug testing notice: (i) 30 days for domestic traditional Chinese medicines; and (ii) three months for imported traditional Chinese medicines.	Specified for the central and local drug regulatory authorities: (a) acceptance of application and preliminary review: five days; (b) local drug regulatory departments sending review opinions, inspection report and application dossiers to the central authority, and notifying the applicant of the review opinions: 30 days from the date an application is accepted; (c) sample testing and specifications verification by a drug testing institute: 60 to 90 days; (d) technical review by the central authority: 150 to 160 days; and (e) administrative decision making: 20 to 30 days.

Appendix (cont'd)

Key features of registration mechanism for proprietary Chinese medicines in Macao, Taiwan and the Mainland

	Macao	Taiwan	The Mainland
Registration process of proprietary Chinese medicines (cont'd)			
Appeal mechanism against registration decision	Not applicable.	An applicant appealing to CCMP in writing with reasons, literature references and relevant documents, within two months after receiving notice of the decision. Only one application for re-examination is allowed.	(a) An applicant submitting an application with reasons for SFDA's second review within 60 days after receiving the decision; (b) SFDA making and notifying the applicant its decision within 50 days after receiving an application; and (c) SFDA accepting no further application for second review thereof if the original decision is affirmed.

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