Guidance Notes on Application for Certificate for Clinical Trial and Medicinal Test (2015)

According to section 129 of the Chinese Medicine Ordinance ("CMO"), for the purpose of facilitating the conduct of a clinical trial or medicinal test of any proprietary Chinese medicine ("pCm"), the Chinese Medicines Board ("CMB") may, upon application, issue a certificate for clinical trial and medicinal test ("Certificate") [Note 1]. Upon submission of the documents, information, samples and other materials required by the CMB and payment of the prescribed fee, the CMB may issue to the applicant a Certificate subject to such conditions as it thinks fit.

The following requirements are required by the CMB in relation to application for the Certificate:

1 Requirements for the person applying for the Certificate ("the applicant"):

a. **For medicinal test,** the applicant should either be the principal investigator or sponsor of the test (or an authorized person of the company or institution);

b. **For clinical trial,** the applicant should either be the sponsor or sponsor-investigator of the clinical trial.

According to the Good Clinical Practice for Proprietary Chinese Medicines ("GCP"), "sponsor" refers to an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial. On the other hand, "sponsor-investigator" refers to an individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

2 The principal investigator should possess the professional knowledge and experience required by the protocol. In the case of a clinical trial, the principal

[Note 1] If the investigational pCm is manufactured by a pCm manufacturer in Hong Kong and is not registered under section 121 of the CMO, an application for exemption under section 158(1) of the CMO from pCm registration should be made to the CMB. If the pCm is manufactured by a local manufacturer, the manufacturer should also apply to the CMB for exemption under section 158(1) of the CMO.

investigator should either be a registered medical practitioner [Note2] or a registered Chinese medicine practitioner [Note3] with ample experience in conducting clinical trials.

3 There should be sufficient and suitable manpower, facilities and equipment in an institution where a **medicinal test** is conducted. If the test is expected to cause pain on a living vertebrate, a licence issued under the Animals (Control of Experiments) Ordinance (Cap. 340) should be obtained by the applicant as a proof to show that the test objectives and treatment of animals (in particular pain control) conform to the requirements of that Ordinance.

4 The facilities and conditions of an institution where **clinical trials** are conducted should allow the trials to be conducted safely and effectively. The institution should either be a hospital or a clinic under the management control of the Hospital Authority/a hospital/an university. The clinical trial site should have equipment and facilities, research professionals (including registered Chinese medicine practitioner), number of beds and number of trial subjects etc. that are adequate and relevant to the trial protocol and a clinical trial management system in place. In addition, an independent Ethics Committee should be established within the institution and be responsible for reviewing clinical trial protocols to ensure compliance with ethical principles and ensuring the safety, well-being and rights of the trial subjects. The composition of the Ethics Committee should conform to the requirements under the GCP stipulated by the CMB; and should include medical professional, non-medical or non-scientific persons, legal expert and a person independent of the clinical trial institution/trial site. The Ethics Committee should consist of at least five members including both gender and have collectively the qualifications and experience to review and assess the scientific, medical and ethical aspects of the proposed trial.

5 Clinical trials of all phases should be conducted in compliance with GCP. The Chinese Medicines Committee (CMSC) will assess the applications with the delegated authority from the CMB under section 157 of the CMO.

[Note 2] A registered medical practitioner means an individual who fulfils the meaning of a "registered medical practitioner" under the Medical Registration Ordinance (Cap. 161).

[Note 3] A registered Chinese medicine practitioner means an individual who fulfils the meaning of a "registered Chinese medicine practitioner" under the CMO (Cap. 549) and the conditions imposed upon a Chinese medicine practitioner with limited registration must allow conducting clinical research at the institution where clinical research is conducted.

6 An applicant is required to submit the following information [Note4]:

a. For medicinal tests:

(i) A duly completed application form and checklist;

(ii) A letter signed by the principal investigator confirming his participation in the medicinal test concerned;

(iii) Curriculum Vitae of the principal investigator;

(iv) Proposed protocol for the medicinal test;

(v) Copy of the animal experiment licence issued under the Animals (Control of Experiments) Ordinance (Cap. 340), when the test is expected to cause pain on a living vertebrate;

(vi) Master formula of the investigational pCm; and

(vii) Label of the investigational pCm and a clear photograph of its sample showing its true colours.

b. For clinical trials:

(i) A duly completed application form and checklist;

(ii) Proposed protocol for the clinical trial;

(iii) Chinese version or Chinese-English bilingual version of the proposed trial information on the trial and informed consent form for trial subjects;

(iv) A letter signed by the principal investigator confirming his participation in the clinical trial concerned;

(v) Curriculum Vitae of the principal investigator and a copy of relevant certificate of registration;

(vi) A letter signed by the Chinese medicine practitioner confirming his participation in the clinical trial concerned and a copy of his certificate of registration (not applicable if the CMP is the principal investigator);

(vii) Document issued by the Ethics Committee of the institution where the trial will be conducted substantiating its approval for the trial to be conducted at that institution (may be submitted within 3 months from the date of application);

(viii) Investigator's brochure (including the pharmacological and toxicological information of the investigational pCm). If the investigational product is a registered pCm, the CMB may consider the substitution of part of the investigator's brochure with information contained in the package insert of the registered pCm;

[Note 4] The applicant may submit application for medicinal test and clinical trial at the same time and provide the corresponding required documents separately. Copies of the same document and information may be provided in one of the two sets of documents if applicable.

(ix) Documentation evidence showing all manufacturers involved in the manufacturing of the investigational products (including the investigational pCm, comparators, placebos, etc.) comply with the Hong Kong Good Manufacturing Practice Guidelines for Proprietary Chinese Medicines ("GMP") or equivalent (not applicable to registered pharmaceutical products);

(x) Master formula of the investigational product(s) (not applicable to registered pharmaceutical products. For registered pCms, the master formula may be submitted by the manufacturer or holder of certificate of registration on behalf of the applicant)*;

(xi) Test reports on heavy metals and toxic elements, pesticide residues and microbial limit of the investigational pCm*;

(xii) Manufacturing method of the investigational pCm *;

(xiii) Product specifications and its drafting note, testing methods and certificate of analysis of the investigational pCm, product specifications and certificate of analysis of the placebo(s)*;

(xiv) Stability test report of the investigational pCm (certified by a GMP-compliant manufacturer or a laboratory recognized by the Chinese Medicines Board)*;

(xv) Label of the investigational product(s) and a clear photograph showing true colours of its sample; and

(xvi) Approval document(s) and information regarding the same clinical trial conducted outside Hong Kong / in other countries (if any).

<u>The following documents are also required if a Certificate was previously issued for the clinical trial which has expired or is about to expire:</u>

(xvii) Clinical Trial Yearly Progress Report /Clinical Trial final report (please state reasons if reports are not submitted or if the trial has not commenced).

<u>The following information is also required if the clinical trial concerned has been approved by the National Medical Products Administration ("NMPA"):</u>

(xviii) The clinical trial approval document or relevant supporting document (may be submitted within 3 months from the date of application); and

(xix) A copy of the trial protocol submitted to the NMPA.

* If an applicant declares on the application form that findings of the clinical trial will not be used in application for pCm registration or variation of registered particulars of registered pCms (e.g. indications and target users of the pCm) and the applicant for the clinical trial is a sponsor-investigator, the Chinese Medicines Board may consider granting an exemption for submission of these documents.

c. The CMSC may, if considered necessary, require the applicant to submit other documents or information, or the original copy of any document for verification.

7 Submitting the application

An applicant should submit the duly completed application form and the required documents:

a. by post; or
b. in person to the Chinese Medicine Regulatory Office of the Department of Health during office hours; or
c. Submit application via electronic forms (Applicable to holders of recognised digital certificates only) (https://eform.cefs.gov.hk/form/dh0056/en/).

After receiving the application, the Chinese Medicine Regulatory Office of the Department of Health will issue a General Demand Note to the applicant. The application fee for the Certificate is HK$2,440. The applicant can make payment according to the payment methods stated in the General Demand Note. Any paid application fee will not be refunded regardless of whether the application is approved.

8 Issuance of an acknowledgement letter

Upon receipt of an application, the Chinese Medicine Regulatory Office of the Department of Health will issue an acknowledgement letter to the applicant confirming his application is being processed. The acknowledgement letter will state the reference number of the application, which should be quoted by the applicant when making any enquiries in relation thereto.

9 Determination of the Application

If the application for the Certificate is approved, the Chinese Medicine Regulatory Office of the Department of Health will issue a General Demand Note to the applicant. The Certificate fee is HK$79. The applicant can make payment according to the payment methods stated in the General Demand Note. Upon payment of the Certificate fee, the Certificate will be sent by registered post unless the applicant has indicated for collection of the Certificate from the Chinese Medicine Regulatory Office of the Department of Health in person. The applicant may choose to receive an electronic copy of the Certificate by email for successful application in addition to the printed Certificate. The Certificate's validity and the conditions/restrictions imposed will be stated thereon.

The issuance of the Certificate is normally 5 months after receipt of the duly completed application form and all necessary documents to show compliance with CMB requirements.

If an application for the Certificate is refused, the CMSC will notify the applicant in writing with reasons for refusal set out thereon. Any applicant aggrieved by the decision made by the CMSC may request, in accordance with section 140 of the CMO, the CMB to review the decision. Such a request shall state the reasons relied upon and be made within 14 days after the receipt of the notification of decision.

10 Variation of information

When there are any changes to be made to the information in relation to the applicant or submitted information during the processing of the application, please inform the Chinese Medicine Regulatory Office of the Department of Health in writing (by post or fax) as soon as possible.

For Certificate holders who wish to apply for variation of information submitted, he should inform the CMB in writing together with details of the requested amendment, addition or deletion and submit the relevant supporting documents (e.g. approval from the Ethics Committee of the institution) at least 1 month prior to the effective date of the variation.

11 Obtaining application forms

Application forms for the certificate for clinical trial and medicinal test can be obtained from:

a. the Chinese Medicine Regulatory Office of the Department of Health during office hours
b. the Chinese Medicine Council of Hong Kong website at : https://www.cmchk.org.hk/pcm/eng/#main_down02.htm

12 Contact address and office hours

Contact address:	16/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon
Office hours:	Monday to Friday (9:00 a.m. to 5:30 p.m.) Saturdays, Sundays and general holidays (Closed)

13 Enquires

For enquires relating to the content of this Guidance Notes, please contact the Chinese Medicine Regulatory Office of the Department of Health:

Email: cmro_ctt@dh.gov.hk
Enquiry hotline: 3904 9130
Fax number: 2319 2664