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

Guidance Notes on the Application for Certificate for Clinical Trial/Medicinal Test

Background

1. Under Regulation 36B (the regulation) of the Pharmacy and Poisons Regulations, a Certificate for Clinical Trial/Medicinal Test (the certificate) is required for the purpose of conducting a clinical trial on human beings or a medicinal test on animals. The regulation only applies to pharmaceutical products[1].

2. The Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee (the Committee) established under the Pharmacy and Poisons Board of Hong Kong is the statutory body to issue the certificate. The Committee adopted the definition of "clinical trial" given in the International Council for Harmonisation Guideline for Good Clinical Practice (ICH GCP) which is defined as "any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy". The Committee issues the certificate through two mechanisms, namely, the Standard Scheme and the Listed Scheme.

Which scheme to apply?

Clinical Trial

3. When the sponsor[2] of a clinical trial is a pharmaceutical company or research organisation/institution, the application for the certificate should be submitted under the Standard Scheme.

4. For clinical trials which are initiated and conducted by a sponsor-investigator[3], the sponsor-investigator should conduct a risk assessment to grade the clinical trial into one of the three categories (i.e. Type A, B or C) by taking into consideration the registration status of the

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[1]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.

[2]Sponsor means an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

[3]Sponsor-investigator means 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 term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

drug and the risk level as compared to the standard medical care. To assist the sponsor-investigator to grade the clinical trial, please refer to Table 1 for reference and the sponsor-investigator should base on the result of the three-risk-level categorisation when deciding whether the application for the certificate should be submitted under the Standard Scheme or the Listed Scheme.

How to assess the risk of a clinical trial initiated and conducted by a sponsor-investigator based on the three-risk-level categorisation?

Applicant should know the potential risk of the trial and make appropriate choice of which scheme, i.e. Standard or Listed, to be applied for. Some examples are listed out in the table below for reference. Please note that if the Listed Scheme is chosen under 4.2.2 and 4.2.3 of Type B, consideration by the Committee is required.

Table 1 – Three-risk-level Categorisation

Clinical trial categories based on the potential risk associated with the drug used				**Processing mechanism**
4.1	**Type A: No higher than the risk of standard medical care.**			
	Examples: Trials involving drug registered in Hong Kong if: (a) they relate to the licensed range of indication, dosage and form; or (b) they involve off-label use which is an established practice and supported by sufficient published evidence and/or guidelines.	4.1.1	In general, the application should be submitted under the Listed Scheme.	Listed Scheme
4.2	**Type B: Somewhat higher than the risk of standard medical care.**			
	Examples: Trials involving drug registered in Hong Kong if: (a) the drug is used for a new indication (different patient population/disease group); or (b) substantial dosage modifications are made for the licensed indication; or (c) the drug is used in combination in which interactions are suspected.	4.2.1	If there is extensive clinical experience with the drug and no reason to suspect a different safety profile in the trial population, the application is considered Type A.	Listed Scheme

		4.2.2	If there is no extensive clinical experience with the drug as indicated in 4.2.1, the applicant can choose to submit the application under the Standard Scheme or the Listed Scheme. However, if the applicant chooses to submit under the Listed Scheme, **the Committee will then consider the individual trial on its own merits and make the final decision on whether the application can be proceeded under the Listed Scheme.**	Listed Scheme or Standard Scheme
	Examples: Trials involving drug not registered in Hong Kong and there is extensive class data or pre-clinical and clinical evidence of the drug.	4.2.3	The applicant can choose to submit the application under the Standard Scheme or the Listed Scheme. However, if the applicant chooses to submit under the Listed Scheme, **the Committee will then consider the individual trial on its own merits and make the final decision on whether the application can be proceeded under the Listed Scheme.**	Listed Scheme or Standard Scheme
4.3	**Type C: Markedly higher than the risk of standard medical care.**			
	Examples: Trials involving drug not registered in Hong Kong.	4.3.1	In general, the application should be submitted under the Standard Scheme.	Standard Scheme

5. For application submitted under the Listed Scheme, the sponsor-investigator should provide the details of the assessment of the trial with justification in the application dossier. Please refer to Appendix 1 for more information when considering whether application for a clinical trial should be submitted under the Listed Scheme.

Medicinal Test

6. Application for a medicinal test should be submitted under the Standard Scheme.

Who should be the applicant?

7. For application submitted under the Standard Scheme, a local company holding relevant licence(s) such as the Wholesale Dealer Licence, Antibiotics Permit and Wholesale Dealer's Licence to supply Dangerous Drugs, whenever applicable, or the principal investigator who conducts the trial should be the applicant.

8. For application submitted under the Listed Scheme, only the sponsor-investigator who initiates and conducts the trial should be the applicant.

How to obtain the application form?

9. Application form is available by:

9.1 Visiting the Drug Evaluation and Import/Export Control Division of Drug Office during office hours.

Address:	Drug Office, Department of Health Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon	
Office hours:	Monday to Friday	9:00 am – 1:00 pm 2:00 pm – 5:45 pm (up to 6:00 pm on Monday) (shroff closes at 15 minutes earlier than the office hours)

9.2 Downloading from the website of Drug Office at http://www.drugoffice.gov.hk.

What to submit?

The Standard Scheme

10. Application submitted under the Standard Scheme should contain:

For all studies, the following documents:

10.1 A completed application form.

10.2 A completed checklist.

10.3 A cover letter listing all the submitted documents.

10.4 A letter from the principal investigator confirming his involvement in the clinical trial or medicinal test.

10.5 The Curriculum Vitae of the principal investigator.

10.6 In case of a clinical trial, documentary evidence proving that the clinical trial has been approved by the Ethics Committee of the institution where it will be conducted (this may be submitted when available at a later date).

10.7 In case of a clinical trial, the proposed patient information and the patient consent form, in both English and Chinese, or in Chinese only.

10.8 A copy of the proposed protocol for the clinical trial or medicinal test.

10.9 Information of the drug (e.g. investigator's brochure, package insert, other information if applicable, etc.).

10.10 A sample certificate of the analysis of the drug.

10.11 Evidence proving that the drug is manufactured in accordance with Good Manufacturing Practices (GMP) (e.g. copy of GMP certificate of the drug manufacturer).

For studies in which a certificate was issued previously and will expire, the following additional documents:

10.12 A copy of the previous certificate.

10.13 Clinical trial progress report(s) (if not available, please provide justification; if the trial has not been started, please also provide justification).

For studies which are also the subject of an application for approval by the National Medical Products Administration (NMPA), the following additional documents:

10.14 Drug clinical trial approval document (臨牀試驗通知書) issued by NMPA (this may be submitted when available at a later date).

10.15 A copy of the protocol submitted to NMPA.

The Listed Scheme

11. Application submitted under the Listed Scheme should contain:

For all studies, the following documents:

11.1 A completed application form.

11.2 A completed checklist.

11.3 A cover letter listing all the submitted documents.

11.4 A completed clinical trial risk assessment form.

11.5 Documentary evidence proving that the clinical trial has been approved by the Ethics Committee of the institution where it will be conducted (this may be submitted when available at a later date).

11.6 The proposed patient information and the patient consent form, in both English and Chinese, or in Chinese only.

11.7 A copy of the proposed protocol.

For studies in which a certificate was issued previously and will expire, the following additional documents:

11.8 A copy of the previous certificate.

11.9 Clinical trial progress report(s) (if not available, please provide justification; if the trial has not been started, please also provide justification).

12. The above lists of documents are not exclusive. The applicant may be required to submit additional or updated documents to support the application. Documents may be submitted in electronic format in a CD-ROM, in addition to the paper copy.

When to submit the application for ongoing clinical trial?

13. In order to avoid interruption of the ongoing clinical trial, applicants are advised to submit a new application **not later than 4 months** before the expiry of the current CTC. Late submission of application and/or provision of incomplete information may cause delay in issue of CTC.

[Important Note: According to Regulation 36B of the Pharmacy and Poisons Regulations (Cap. 138A), a person must not conduct a clinical trial on human beings or a medicinal test on animals, or cause or permit such a trial/ test to be conducted, except in accordance with a valid clinical trial certificate/ medicinal test certificate issued by the Pharmacy and Poisons Board. Any person who contravenes the above commits an offence and is liable to a fine at level 2 (currently is HK$5,000).]

How to submit the application?

14. Application should be submitted in person at, or by mail to the Drug Evaluation and Import/Export Control Division of Drug Office. It will be acknowledged by receipt upon payment of the application fee (currently HK$1,420). If payment is made by cheque, the cheque should be made payable to "The Government of the Hong Kong Special Administrative Region" or "The Government of the HKSAR" and crossed. The acknowledgement receipt will contain an application number and the applicant may quote it when making an enquiry regarding the application.

How to collect the certificate?

15. When the application is approved, the applicant will be notified in writing. Payment of the certificate fee (currently HK$1,420) and collection of certificate should be made in person at

the Drug Evaluation and Import/Export Control Division of Drug Office during office hours. If payment is made by cheque, the cheque should be made payable to "The Government of the Hong Kong Special Administrative Region" or "The Government of the HKSAR" and crossed.

How to make enquiries?

16. Should applicants have enquiries on how to make an application for a clinical trial or medicinal test, or on progress of the submitted applications, please contact the Drug Evaluation and Import/Export Control Division of the Drug Office by phone or fax:

Enquiry phone no.:	(852) 3974 4175
Fax no.:	(852) 2803 4962

Collection of personal data

17. Regarding the collection of personal data, please refer to "Statement of Purposes" at Appendix 2 for more information.

Drug Evaluation and Import/Export Control Division
Drug Office
Department of Health

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Appendix 1

This appendix includes some examples to facilitate the applicant when considering whether application for a clinical trial should be submitted under the Listed Scheme. The applicant should apply the principles illustrated in the below examples for the risk assessment and provide supporting document as justification.

<u>Example (1)</u> – Trials involving drug registered in Hong Kong and they relate to the licensed range of indication, dosage and form, i.e. 4.1(a) in Table 1.

Q: A sponsor-investigator initiates a clinical trial to investigate the cost-effectiveness of Drug X versus Drug Y in patients with chronic hepatitis B in the local setting. Drug X and Drug Y are registered in Hong Kong. In the trial, the drugs are used in accordance with the approved indication, dosage and form as stated in the package inserts. Can this trial be submitted under the Listed Scheme?

A: The above trial can be submitted under the Listed Scheme (see 4.1.1).

When submitting under the Listed Scheme, the applicant should choose rationale "C1" and explain the details of the risk assessment in part C of the risk assessment form. A copy of the package insert of Drug X and Drug Y should also be submitted as supporting evidence.

<u>Example (2)</u> – Trials involving drug registered in Hong Kong and they involve off-label use which is an established practice and supported by sufficient published evidence, i.e. 4.1(b) in Table 1.

Q: A sponsor-investigator initiates a clinical trial to investigate the effect of Drug X on prophylaxis against candidal infection in paediatric patients. Drug X is registered in Hong Kong. In the trial, the drug is used in a dose which is higher than the approved dose. The higher dose is chosen according to reputable clinical guidelines published in the paediatric field. Can this trial be submitted under the Listed Scheme?

A: The above trial can be submitted under the Listed Scheme (see 4.1.1).

When submitting under the Listed Scheme, the applicant should choose rationale "C2" and explain the details of the risk assessment in part C of the risk assessment form. A copy of the concerned guidelines should also be submitted as supporting evidence.

<u>Example (3)</u> – Trials involving drug registered in Hong Kong and the drug is used for a different patient population group, i.e. 4.2(a) in Table 1. However, there is extensive clinical experience with the drug and no reason to suspect a different safety profile in the trial population.

Q: Drug X is registered in Hong Kong for treatment of gastrointestinal stromal tumors (GIST) after surgery in patients with high risk of relapse. A sponsor-investigator initiates a clinical trial to investigate the effect of Drug X when given before surgery in patients with GIST. The drug is not used in accordance with the approved indication and there are no clinical guidelines recommending use of Drug X before surgery. However, as the drug is approved for treatment of GIST and it is widely used in the investigator's institution for GIST patients, there is extensive clinical experience and no reason to suspect a different safety profile in the trial population. Can this trial be submitted under the Listed Scheme?

A: The above trial can be submitted under the Listed Scheme (see 4.2.1).

When submitting under the Listed Scheme, the applicant should choose rationale "C3" and explain the details of the risk assessment in part C of the risk assessment form, including explanation of extensive clinical experience with the drug and why there is no reason to suspect a different profile in the trial population.

<u>Example (4)</u> – Trials involving drug not registered in Hong Kong, i.e. 4.3 in Table 1. However, there is extensive class data of the drug.

Q: A sponsor-investigator initiates a clinical trial to investigate the effect of a dose combination of a vitamin and a mineral in some skeletal diseases. However, there is no such dose combination registered in Hong Kong. The investigator sources the drug from an overseas GMP manufacturer. Certificate of analysis of the drug and GMP certificate of the manufacturer are available. There is extensive class data of the vitamin and mineral as they have been commonly used for many years and safety of the combination has well been established. The dosage of the vitamin and mineral used in the trial are also within the usual dosage recommended by reputable drug references. Can this trial be submitted under the Listed Scheme?

A: The above trial may be submitted under the Listed Scheme (see 4.2.3). The Committee will then consider the individual trial on its own merits and make the final decision on whether the application can be proceeded under the Listed Scheme.

When submitting under the Listed Scheme, the applicant should choose rationale "C5" and explain the details of the risk assessment in part C of the risk assessment form. A copy of the certificate of analysis, GMP certificate and concerned drug references should also be submitted as supporting evidence.

<u>Example (5)</u> – Trials involving the use of placebo.

Q: A sponsor-investigator initiates a clinical trial which include a placebo-controlled arm. The placebo is manufactured by a GMP manufacturer. Certificate of analysis of the placebo and GMP certificate of the manufacturer are available. Can this trial be submitted under the Listed Scheme?

A: If other prerequisites for submission of application under the Listed Scheme has been met, the above trial can be submitted under the Listed Scheme as placebos are generally not required to be registered in Hong Kong.

When submitting under the Listed Scheme, a copy of the certificate of analysis and GMP certificate should be submitted to support the quality of the placebo.

<u>Example (6)</u> – Trials involving healthy subjects or patients without the targeted diseases.

Q: A sponsor-investigator initiates a clinical trial to investigate the effect of a locally registered vaccine for prevention of flu in school children. In the trial, the vaccine is used in accordance with the approved label. As the vaccine is indicated for prevention of the disease, the trial subjects are generally healthy. Can this trial be submitted under the Listed Scheme?

A: The above trial can be submitted under the Listed Scheme. The use of the vaccine in the trial is to prevent flu (not to treat flu) in trial subjects and therefore no higher risk is induced to them as compared with having flu shot at their family physicians. .

<u>Example (7)</u> – Bioequivalence/bioavailability (BABE) trials involving healthy volunteers.

Q: A sponsor-investigator initiates a BABE trial of two locally registered drugs which recruits healthy volunteers. Can this trial be submitted under the Listed Scheme?

A: The above trial **cannot** be submitted under the Listed Scheme. BABE trials and other related trials such as pharmacokinetic (PK) and pharmacodynamic (PD) trials of locally registered drugs recruiting healthy volunteers should not be submitted under the Listed Scheme. The administration of the drugs is to verify how the human body handles the drugs and additional risk is induced to the trial subjects who will not be benefited at all.

Appendix 2

Statement of Purposes

Purpose of Collection

1. The personal data provided by certificate applicants are for the purposes of application for certificate under the Pharmacy and Poisons Ordinance. The personal data provided will be used by the Department of Health for the following purposes:

(a) Proof of eligibility for a certificate

(b) Assessment of whether the applicant is a fit and proper person to be granted a certificate

2. The provision of personal data is voluntary. If you do not provide sufficient information, we may not be able to prove your eligibility for a certificate, or to assess whether you are a fit and proper person to be granted a certificate.

Classes of Transferees

3. The personal data you provide are mainly for use within the Department of Health and the Pharmacy and Poisons Board. Apart from this, the data may only be disclosed to parties where you have given consent to such disclosure or where such disclosure is allowed under the Personal Data (Privacy) Ordinance.

Access to Personal Data

4. You have a right of access and correction with respect to the personal data as provided in sections 18 and 22 and Principle 6 of Schedule 1 of the Personal Data (Privacy) Ordinance. Your right of access includes the right to obtain a copy of your personal data. A fee may be imposed for complying with a data access request.

Enquiries

5. Enquiries concerning the provided personal data, including the making of access and corrections, should be addressed to:

Senior Pharmacist
Drug Evaluation and Import/Export Control Division
Drug Office, Department of Health
Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East,
100 How Ming Street, Kwun Tong, Kowloon
Tel: 3974 4175