

**Baker
McKenzie.**

CLINICAL TRIALS HANDBOOK Asia Pacific



HONG KONG

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Hong Kong

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Introduction

The main regulator of clinical trials in Hong Kong is the Department of Health (DOH).

Other regulators include the following:

- The ethics committee of the Hospital Authority's (HA) relevant operating cluster to which the public hospital or research institution belongs ("**Cluster**") or the private hospital in which the trial is to be conducted ("**Ethics Committee**")
- The Medical Council of Hong Kong and the Chinese Medicine Council of Hong Kong, which investigate noncompliance by medical practitioners and Chinese medicine practitioners with the Code of Professional Conduct in conducting clinical trials
- The Customs and Exercise Department (C&E), which issues licenses for importing controlled chemicals for use in clinical trials
- The Office of the Privacy Commissioner for Personal Data, which regulates the use and storage of personal data

Regulatory framework

- (a) *Section 29(qb) of the Pharmacy and Poisons Ordinance (Cap 138), and regulation 36B of the Pharmacy and Poisons Regulations (Cap 138A)*
 - A Clinical Trial Certificate from the DOH is required to conduct clinical trials on human beings and medicinal tests on animals in Hong Kong.
- (b) *Section 129 of the Chinese Medicine Ordinance (Cap 549)*
 - A Clinical Trial Certificate from the Chinese Medicines Board of the DOH is required to conduct clinical trials involving proprietary Chinese medicine.
- (c) HA's Guide on Research Ethics for Study Site and Research Ethics Committee and Investigator's Code of Practice
 - Governing study sites, research ethics committee and investigators of clinical trials involving public hospitals (as study site), their staff and patients
 - Expressly adopted principles of the Declaration of Helsinki and the ICH GCP (whenever applicable) as mandatory ethical requirements
- (d) Standard Operating Procedures (SOP) from the relevant Cluster Ethics Committee
 - Specifies documents required and criteria for ethics approval, renewals, and circumstances for suspension or termination of any clinical trial

- (e) Code of Practice for Private Hospitals, Nursing Homes and Maternity Homes issued by the DOH for clinical trials in private hospitals
 - Specifies the setting up of an Ethics Committee to approve, review and monitor clinical trials at their site, and the compliance with the code as a condition for the registration and re-registration of private hospitals
- (f) *Sections 6C(1) and 6D(1) of the Import and Export Ordinance (Cap 60) and Section 3 of the Control of Chemicals Ordinance (Cap 145)*
 - Obtain necessary import licenses to import test articles or control chemicals into Hong Kong for clinical trials
- (g) *Personal Data (Privacy) Ordinance (Cap 486) (PDPO)*
 - Specifies rules and principles regulating the use and storage of personal data

The regulatory framework is basically the same for trials involving molecule-based Investigative Medical Products (IMPs) or study drugs and biological-based IMPs. Different import and export licenses may be required, depending on the nature of the test articles.

Clinical Trial Certificates

With effect from 1 May 2014, an application for a Clinical Trial Certificate may be made under the Standard Scheme or the Listed Scheme. The Listed Scheme provides a simplified mechanism to facilitate the processing of applications for low-risk clinical trials, and is available to clinical trials initiated and conducted by sponsor-investigators (excluding corporations or agencies). A sponsor-investigator is responsible for conducting a risk assessment on the clinical trial in deciding on the applicable scheme. Generally, where a clinical trial involves a registered drug in Hong Kong and there is support that the proposed use carries no higher than the risk of standard medical care, the Listed Scheme may be used.

This is not available, however, to applications for clinical trials involving proprietary Chinese medicine. Applications for Certificate for Clinical Trial of proprietary Chinese medicine should be made to the Chinese Medicines Committee of the DOH.

If the sponsor of a clinical trial is a pharmaceutical company or research organization, the application should be submitted under the Standard Scheme.

Clinical trial agreements (CTAs)

The following permissions/notifications are required to conduct a trial:

- A Clinical Trial Certificate issued by the DOH
- Approval by the Legal Services Section of the HA of the CTA (or under process) with an approved Letter of indemnity (or under process) for sponsored trials or where commercial interest is involved
- Administrative approval from the study site/hospital management
- Ethics approval from the relevant Ethics Committee prior to clinical trials and when deviation or changes from the approved protocol are required

- Import/export license for test articles involved in the clinical trials from C&E or DOH as the case may be

The HA may require the trial to be reviewed and approved by a committee in addition to the Ethics Committee for certain clinical trials, such as those involving any of the following:

- The administration of radioactive substances on humans
- Tissues from human fetuses
- Transfer of genetic material to human subjects
- All devices, whether investigational or marketed

The principal investigator is responsible for obtaining approval for conducting the clinical trial from the relevant Ethics Committee and for coordinating the approval of the CTA from the HA's Legal Services Section. The party initiating the clinical trial, which can be the sponsor or the investigator, will be responsible for applying for the Clinical Trial Certificate.

Once the Clinical Trial Certificate is granted, the initiator (sponsor or investigator) will then apply for an Import and Export License to obtain the test articles for the actual clinical trial (if necessary).

For sponsored clinical trials, it is the sponsor that has to purchase insurance. A copy of the certificate of insurance may also be required, depending on the relevant Ethics Committee, investigator or the Contract Research Organization (CRO). The research institution may be required by the sponsor in the CTA to maintain insurance to cover any liability to the sponsor and subjects as a result of its breach of obligation in relation to the clinical trial. The HA provides a template for a standard indemnity that requires the sponsor to indemnify the HA, the study site and the principal investigator for the following:

- Losses or liabilities suffered as a result of a breach of obligations or negligence of the sponsor or CRO
- Legal costs incurred by the HA in reporting any death in the Coroner's Inquest, dealing with police investigations, and dealing with the media or other governmental agencies
- Actual costs incurred by the HA in providing treatment to the study patient as a result of participating in the study

The sponsor must also provide a lawyer to those indemnified for dealing with any claims they may receive arising out of the clinical trial.

An indemnity, bond, or insurance from the sponsor covering the above is a requirement to obtain administrative and ethics approval for conducting the clinical trial.

For investigator-initiated trials, the investigator will have to assess the risk involved and whether or not insurance should be purchased. For example, in trials where the study may simply be a questionnaire, the investigator may be of the opinion that insurance is not necessary as the risks associated with a questionnaire are low. However, the Ethics Committee may require an investigator to secure insurance for covering a clinical study with higher than nominal risk.

Generally, the study site should not bear any risks of the study. However, the indemnity from the sponsor will often exclude liabilities arising from negligence, malpractice or violation of the protocol by those indemnified.

Clinical trials of all phases require the Clinical Trial Certificate and ethics approval. The review by the Ethics Committee may generally be more stringent in Phase I trials as opposed to Phases II, III and IV. Phase I trials are also

subject to additional requirements in relation to ethics oversight and scientific evaluation. Also, some Cluster Ethics Committee exempt Phase IV clinical trials from an application fee for the ethics review.

Sponsor and CROs

The sponsor can be an individual, a company, an institution or an organization that initiates, finances and indemnifies the HA, the investigator and the institution regarding the clinical trial. The sponsor is usually the manufacturer of the study drug. Often, sponsors do not actually manage the clinical trial and instead distribute the study drugs to an investigator who directs the conduct of the trial.

The sponsor needs to be in Hong Kong. An overseas company is not eligible to apply for a Clinical Trial Certificate.

If the sponsor is not within Hong Kong, it will need to apply for a Clinical Trial Certificate through a Hong Kong-registered company or a Hong Kong-registered medical doctor or Chinese medicine practitioner. The responsibilities of the local representative will be the same as those of the sponsor, whenever applicable.

Sponsors have the ultimate responsibility for the clinical trial of the test articles and for ensuring compliance with laws and regulations. Sponsors are allowed to contract their responsibilities of project management, finance and legal monitoring, data management, statistical analysis, medical writing, and education to a CRO. There are no legal requirements governing the choice and/or appointment of a CRO.

Where the clinical trial is sponsored or where there is a commercial interest involved, the HA will require a draft CTA to be submitted to the head of all implicated departments at the study site, and to its Legal Services Section, prior to the grant of the administrative approval by the site. The Ethics Committee can also request a copy of the CTA for its review in examining the application for ethics approval.

Investigator

The investigator is a person responsible for conducting the clinical trial at the study site. The investigator must be a medical doctor registered as a medical practitioner with the Medical Council of Hong Kong or a Chinese medicine practitioner registered with the Chinese Medicine Council of Hong Kong. The function of the investigator is to perform the study on the study drug for the sponsor according to the description of the study. When applying for a Clinical Trial Certificate, the investigator is required to submit a brochure with information on the new drug. A principal investigator must be appointed and a letter from him is required to confirm his involvement in the trial.

The general responsibilities of the investigator are to protect human subjects, comply with regulatory, ethical and institutional requirements on research conducts, and ensure fair conduct and the fair reporting of clinical trials. As the principal investigator is accountable to the sponsor and the study site (the HA or the university in which the clinical trial is held) for all activities relating to the clinical trial, he must also ensure that the trial is scientifically sound and ethically justified, and he must manage the research project and supervise the research team.

Investigators need to monitor the safety of the subjects throughout the study. The principal investigator is responsible for reporting to the following any adverse events that may be regarded as caused by the study drug:

- The Adverse Drug Reaction Monitoring Unit of the DOH
- The sponsor
- The relevant Ethics Committee
- HA's Legal Services Section, if there are any potential legal implications

Study drugs

The authorizations required to administer the study drug in Hong Kong are as follows:

- (a) A Clinical Trial Certificate from the DOH, which is valid for five years
- (b) An Import License to obtain the study drugs for the clinical trial if the study drug needs to be imported into Hong Kong
- (c) An additional license from the C&E for importing into Hong Kong study drugs that contain any of the following five controlled chemicals as pharmaceutical raw materials (active pharmaceutical ingredients): ephedrine, ergotamine, ergometrine, pseudoephedrine, norephedrine (phenylpropanolamine) and their salts.

Sponsors are not legally obliged to provide study drugs for free or finance medical procedures, but the usual practice is that study drugs are provided by the sponsor and/or the drug manufacturer without charge. The trial subjects generally do not need to pay for the study drugs. Clinical trials conducted under a local research grant or funded by universities may have reimbursement arrangements between the investigator and the drug manufacturer.

There are no specific rules in legislation regarding liability for clinical trials. Liabilities may therefore be found in contractual arrangements and in tort. The sponsor will usually not be liable for malpractice, negligence or violation of the Study Protocol by the HA, the participating university, hospital or the principal investigator, as these have been excluded in most of the indemnities.

The HA, the participating university or hospital may have vicarious liability for the malpractice of the investigator, while the investigator can be subjected to professional disciplinary proceedings and legal proceedings.

The HA provides standard indemnities that can be signed as a separate document. It is advisable, however, that indemnity clauses (or reference to separate indemnities) be included in the CTA or its appendices so that parties are clear on the existence of the scope of the indemnities.

Other than the above, for sponsor-initiated trials, the sponsor will usually be ultimately liable for the study.

There are no specific requirements relating to the publication of study results. Any requirements relating to an individual clinical trial should be detailed in the Study Protocol or the CTA. Certain institutions may insist on a certain manner of publication in the Study Protocol or the CTA. Any use and storage of the subjects' personal information should be within the scope of the written consent and in accordance with the PDPO.

Internal publications in the form of progress reports on clinical trials are required on a yearly basis, and a final study report at the end of the study is to be submitted to the DOH by the principal investigator. The DOH and the HA both provide templates for such reports.

The yearly progress report must cover the following:

- (a) Start and anticipated end date of the clinical trial
- (b) Number of patients (target number and number of patients recruited)
- (c) Number of patients that have completed the clinical trial
- (d) Number of patients that have dropped out of the clinical trial and the reasons for dropping out
- (e) Any changes for the principal investigator
- (f) Summary of amendments during the report period (if any)

- (g) Summary of serious adverse events (if any)
- (h) Summary of complaints about the study (if any)
- (i) Summary of recent findings (especially information about risks associated with the research)
- (j) Whether the progress of study is according to plan, the study period must be extended, or the study has been prematurely terminated

In addition to (a) – (d), (g) – (h), and (j), the final report must also cover the following:

- (i) End date of the clinical trial
- (ii) Summary of the study outcome

Trial subjects can be provided with the study drug after the termination of the clinical trial, provided that relevant legal requirements and management and ethical approvals have been obtained. This is a decision made by the principal investigator and the sponsor. Inquiries should be made with the DOH if there is uncertainty on whether there is any legal control for the continuous use of the article after expiry of the clinical trial. Usually, the CTA or protocol will contain provisions regarding whether or not the study drug will be made available to test subjects after the clinical trial.

In general, trial subjects should continue to receive test articles that are proven to be beneficial in their treatment until these articles are made available commercially, especially if they are life-saving or have enormous effect on the trial subject's quality of life, and there is no alternative effective treatment. Arrangement of test article supply or lack of it after termination of the clinical trial should be explained to subjects in the consent process, especially when a test article may not be financed by the public health service due to budgetary reasons (Clause 8 of *HA's Investigator Code of Practice*).

For non-trial subjects, study drugs that are not registered for sale in the market but have been approved for a clinical trial may be administered only if **all** of the following exceptional circumstances are present:

- Subject is facing a life-threatening situation.
- Available treatments are unproven or unsatisfactory, or have failed.
- Subject is not enrolled, or is not eligible to enroll in a trial involving the study drugs within the research time.

Approval for the use of study drugs on non-trial subjects must be sought from the research team and the study site authority, and use must be reported to the relevant Ethics Committee.

Intellectual property (IP) and data

Depending on the contractual clauses in the CTA, the sponsor will generally be entitled to all inventions resulting from the clinical trial. Certain institutions, however, may include in their standard template agreements that they retain the invention and IP rights. The sponsor should check carefully before it signs any agreement or protocol with the institutions.

The following contractual clauses are recommended:

- (a) The sponsor's exclusive ownership of any invention or IP rights created as a result of the clinical trial, and any documents, items and materials provided during the clinical trial, together with all confidential information

and IP rights contained, and that all relevant documents, materials, and items should be returned at the expiry of the trial.

- (b) Any inventions or IP rights created as a result of the clinical trial must be notified and assigned by the principal investigator, the university/institution, and all members of the study team to the sponsor.
- (c) Assignment and waiver from the principal investigator and the university/institution shall occur automatically on creation of the invention.
- (d) The principal investigator and the university/institution shall, and shall procure that all members of the study team take all necessary actions to secure inventions for the benefit of the sponsor, and that all rights to the invention be vested fully and effectively on the sponsor.
- (e) The sponsor has the sole right to file, prosecute, maintain and bring actions relating to patents in relation to any of the inventions arising from the clinical trial.

Investigator-initiated trials are allowed in Hong Kong. Pharmaceutical companies can provide support by, for example, providing study drugs at a discounted price or at no charge.



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