Guidance Notes for Holders of the Certificate for Clinical Trial and Medicinal Test

Part A:

All holders of the Certificate for Clinical Trial and Medicinal Test ("the Certificate") should comply with the following requirements

(1) For Certificate holders conducting medicinal tests, they should :

1 Ensure that the investigational proprietary Chinese medicine ("pCm") is only used for conducting the medicinal test referred to on the Certificate and is not to be used for sale or any other purposes except in the case where the pCm has been approved for registration by the Chinese Medicines Board ("CMB") of the Chinese Medicine Council of Hong Kong under the Chinese Medicine Ordinance (Cap. 549);

2 Retain the usage record of the investigational pCm for inspection when deemed necessary;

3 Inform the CMB in writing of any change in the medicinal test protocol; and

4 Submit, as soon as possible, a summary of the test results, the usage record of the investigational pCm and disposal method of the remaining investigational pCm upon completion of the test (the form at Annex I may be used).

(2) For Certificate holders conducting clinical trials, they should:

1 Ensure that the investigational product is only used for conducting the clinical trial referred to on the Certificate and is not used for sale or any other purposes, except in the case where the pCm has been approved for registration by the CMB under the Chinese Medicine Ordinance (Cap. 549);

2 Ensure that the clinical trial is conducted in compliance with the Good Clinical Practice for Proprietary Chinese Medicines ("GCP") and retain the usage record of the investigational product and documents specified in the "Documentation retained for clinical trial" (Appendix II of GCP) for inspection when deemed necessary;

3 Report to the Chinese Medicine Regulatory Office of the Department of Health of all local drug-related safety reports, i.e. Adverse Drug Reactions ("ADR") reports:

(a) For ADRs that are serious [Note1] and unexpected [Note2], report as soon as possible (the form at [Annex II] may be used);

(i) Fatal or life-threatening unexpected ADRs should be reported to the Chinese Medicine Regulatory Office of the Department of Health as soon as possible but no later than 7 calendar days after first knowledge by the sponsor that a case qualifies, followed by a report as complete as possible within 8 additional calendar days. This report must cover an assessment of the importance and implication of the findings, including relevant previous experience with the same or similar medicinal products.

(ii) Other serious, unexpected ADRs that are not fatal or life-threatening should be reported to the Chinese Medicine Regulatory Office of the Department of Health as soon as possible but no later than 15 calendar days after first knowledge by the sponsor that the case meets the minimum criteria for expedited reporting [Note3].

(b) For non-serious and expected ADRs, it should be reported as a brief summary at the conclusion of the trial.

4 Submit a yearly progress report and a clinical trial final report at the end of the trial. The forms at [Annexes III and IV] may be used;

5 Inform the CMB in writing before terminating the clinical trial and provide the reasons for termination; and

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[Note 1] Serious ADR or adverse event:
A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or causes congenital anomaly/birth defect of foetus.
Medical and scientific judgment should be exercised in deciding whether expedited reporting is required in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These events should also be considered serious in general. Examples of such events include intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse.

[Note 2] Unexpected ADR:
An adverse reaction, the nature or severity of which is not consistent with the existing product information (e.g. investigator's brochure for an unapproved investigational medicinal product, or information leaflet or package insert of an approved medicinal product).

[Note 3] Minimum criteria for expedited reporting:
- an identifiable patient;
- a suspect medicinal product;
- an identifiable reporting source;
- an event or outcome that can be identified as serious and unexpected; and
- for which, in clinical investigation cases, there is a reasonable suspected causal relationship.

6 Inform the CMB in writing at least 1 month prior to the effective date of the proposed variation, together with the relevant supporting documents, of any amendment, addition or deletion of the documents or information (e.g. clinical trial protocol, informed consent form, investigator's brochure, etc.) submitted during the application for the Certificate. If the variation of information relating to the Certificate requires approval from the Ethics Committee of the institution conducting the trial; the approval letter should be submitted with the application for variation. No variation should be implemented prior to the receipt of the CMB acknowledgement in writing that the variation is recorded (see "Part B" for details).

[Note: In cases where the variation of information is unforeseeable by the Certificate holder, he should inform the CMB in writing within 3 working days of first knowledge of that variation, together with supporting documents to substantiate the application and justifications on why the variation was unforeseeable. Please note that the CMB will examine whether the clinical trial is conducted in compliance with the GCP and the trial subjects are protected and determine whether the Certificate is still valid.]

Please submit all forms/reports/documents to the following address: Chinese Medicine Regulatory Office, Department of Health, 16/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon. Fax: 2319 2664

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Part B:

Guidance notes on Application for variation of information after obtaining the Certificate for Clinical Trial and Medicinal Test

According to section 129 of the Chinese Medicine Ordinance, for the purpose of facilitating the conduct of a clinical trial or medicinal test of any proprietary Chinese medicine, the CMB may, upon application, issue a Certificate. On submission of the documents, information, samples and other materials required by the CMB and upon payment of the prescribed fee, the CMB may issue the Certificate which shall be subject to such conditions as it thinks fit.

After the issuance of a Certificate, if the Certificate holder intends to vary any information or documents submitted during the application for the Certificate should follow the arrangements below:

1 Notify the CMB

(a) After a Certificate is issued, if the Certificate holder requires to amend, add or delete documents or information provided to the CMB for assessment, i.e. to vary any documents or information (e.g. the clinical trial protocol, informed consent form, investigator's brochure, etc.) submitted during application for the Certificate, he should inform the CMB in writing at least 1 month prior to the effective date of the proposed variation together with supporting documents.

(b) If the variation of information requires approval from the Ethics Committee of the institution conducting the trial, the Certificate holder should also submit the corresponding approval letter.

(c) If the variation of information involves amendments to the particulars set out on the Certificate, e.g. name and correspondence address of the Certificate holder, the Certificate holder should return the Certificate and provide a written declaration that he is willing to cancel the original Certificate obtained in accordance with section 129 of the CMO after the application for variation of information is approved by the CMB.

(d) If the variation of information is unforeseeable by the Certificate holder, he is required to inform the CMB in writing of the variation, together with supporting documents and justifications for the unforeseeable variation, within 3 working days after first knowledge.

(e) Written notices and the required supporting documents addressed to the CMB should be submitted to the Chinese Medicine Regulatory Office of the Department of Health by post or by hand during office hours.

Address:	16/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon
Office hours:	Mondays to Fridays – 9:00 a.m. to 5:30 p.m. Saturdays, Sundays and general holidays – closed

2 Processing applications for variation of information

Upon receipt of an application, the Chinese Medicine Regulatory Office of the Department of Health will issue an acknowledgement letter to the Certificate holder confirming that the application is being processed. No variation should be implemented prior to the receipt of the CMB acknowledgement in writing that the variation is recorded.

[Note: In cases where variation of information is unforeseeable by the Certificate holder, the CMB will examine whether the clinical trial is conducted in compliance with the GCP and the trial subjects are protected and determine whether the Certificate is still valid.]

3 Announcing application results

(a) When CMB approves the application for variation of information:

(i) The Certificate holder will receive a written notification; or

(ii) When the variation of information involves amendments to the particulars set out on the Certificate, e.g. name and correspondence address of the Certificate holder, the Chinese Medicine Regulatory Office of the Department of Health will issue a General Demand Note to the Certificate holder.

(iii) The Certificate fee is HK$79. The Certificate holder can make payment according to the payment methods stated in the General Demand Note.

(iv) Upon payment of the Certificate fee, an updated Certificate and the written notification for the approval will be issued and sent by registered post. The

Certificate holder may also collect the Certificate and notification letter in person.

(b) When the CMB refuses an application for variation of information, the Certificate holder will receive a notice for refusal of the application for variation of information with reasons of refusal stated thereon.

4 Flowchart on processing of applications

A flowchart on processing of applications for variation of information is shown in ***Figure 1***.

5 Enquiries

For enquiries about the content of this Guidance Notes, please contact the Chinese Medicine Regulatory Office of the Department of Health by phone or by fax:

Enquiry hotline: 3904 9130
Fax number: 2319 2664

收件日期： 檔案編號：

附頁 I

藥物測試報告
Medicinal Test Report

報告期 Report period	至 to		
本報告日期 Date of this report (dd-mm-yyyy)：			
臨床證驗及藥物測試證明書編號 Number of Certificate for Clinical Trial and Medicinal Test :			
方案編號 Protocol no.：			
方案標題 Protocol title：			
開始日期 Start date：	日Day	月Month	年Year
預計結束日期 Anticipated end date：	日Day	月Month	年Year
研究結果的撮要 Summary of study outcome：			

試驗藥物的用藥紀錄 (如多於 1 種試驗藥物，請另頁填寫)：
Record of usage of the investigational product (If more than 1 investigational product, please use a separate sheet):

試驗藥物名稱 Name of investigational product			
供應單位及地址 Name and address of supplier			
收貨數量 Quantity received		日期 Date	
使用後的餘額 Remaining quantity after use		日期 Date	
剩餘試驗藥物的處理方法 Handling of the remaining investigational product			

研究者姓名 Name of Investigator：　　簽署 Signature：

職位 Posting：　　本報告日期 Date：

機構名稱及地址 Name and Address of Organization：

收件日期： 檔案編號：

疑似不良反應報告表格
Suspect Adverse Reaction Report

A 部: 不良反應的資料
PART A: REACTION INFORMATION

1. 病人姓名縮寫(先名後姓) PATIENT INITIALS (first. last) ：	1a. 國家 COUNTRY		
2. 出生日期 DATE OF BIRTH (dd-mm-yyyy)：	2a. 年齡(歲) AGE (Years)		
3. 性別 SEX			
4-6 呈現反應的日期 REACTION ONSET	日 Day	月 Month	年 Year
7 +13 反應的說述(包括相關測試／化驗的日期) DESCRIBE REACTION(S) (including relevant tests/lab date)			
8-12 請剔選所有符合不良反應的說明 CHECK ALL APPROPRIATE TO ADVERSE REACTION ☐ 病人死亡 Patient Died ☐ 當事人入院或延長住院時間 Involved or Prolonged Inpatient Hospitalization ☐ 當事人持續或明顯地出現身體殘障或喪失工作能力 Involved Persistence or Significant Disability or Incapacity ☐ 危及性命 Life Threatening ☐ 胎兒先天畸形 Congenital Anomaly			

B 部: 疑涉藥物的資料
PART B: SUSPECT DRUG(S) INFORMATION

14. 疑涉藥物 SUSPECT DRUG(S)			
14a. 成份及輔料名稱 INGREDIENT AND EXCIPIENT(S)			
15. 每日劑量 DAILY DOSE(S)			
16 給藥途徑 ROUTE(S) OF ADMINISTRATION			
17. 主治用途 INDICATION(S) FOR USE			
18. 治療日期 (由／至) THERAPY DATES (from/to)			
19. 治療期 THERAPY DURATION			
20. 停藥後反應是否消減? DID REACTION ABATE AFTER STOPPING DRUG?	☐是Yes	☐否No	☐不適用N/A
21. 再度用藥後反應是否重現? DID REACTION REAPPEAR AFTER REINTRODUCTION?	☐是Yes	☐否No	☐不適用N/A

C 部: 合併用藥物及病歷

PART C: CONCOMITANT DRUG(S) AND HISTORY

22. 合併用藥物的名稱及施藥日期 (用以治療疑似不良反應的藥物除外) CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. 其他相關病歷 (例如診斷、敏感症、懷孕及上次經期等資料) OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period. etc.)

D 部：製藥商資料

PART D: MANUFACTURER INFORMATION

24a. 製藥商名稱及地址 NAME AND ADDRESS OF MANUFACTURER			
24b. 符合藥品生產質量管理規範證書編號 CERTIFICATE OF GOOD MANUFACTURING PRACTICE NUMBER			
24c. 製藥商接收報告日期 DATE RECEIVED BY MANUFACTURER	日 Day	月 Month	年 Year
24d. 報告來源 REPORT SOURCE	☐ 研究 STUDY ☐ 文獻 LITERATURE ☐ 醫護人員 HEALTH PROFESSIONAL		
25a. 報告類別 REPORT TYPE	☐ 初步報告 INITIAL ☐ 跟進報告 FOLLOWUP		

申報人姓名 Reported by：

簽署 Signature：

職位 Posting：

本報告日期 Date：

機構名稱及地址 Name and Address of Organization：

收件日期: 檔案編號:

臨床試驗年度進度報告

Clinical Trial Yearly Progress Report

報告期 Report period	至 to		
本報告日期 Date of this report (dd-mm-yyyy)：			
臨床證驗及藥物測試證明書編號 Number of Certificate for Clinical Trial and Medicinal Test :			
方案編號 Protocol no.：			
方案標題 Protocol title：			
開始日期 Start date：	日Day	月Month	年Year
預計結束日期 Anticipated end date：	日Day	月Month	年Year

目標病人數目(方案所載) Target no. of patient (as stated in protocol)	
擬招募病人數目(每個地點) No. of patient intended to recruit (per site)	
已招募病人數目(每個地點) No. of patient recruited (per site)	
完成試驗的病人數目(每個地點) No. of patient completed the trial (per site)	
退出試驗的病人數目(每個地點) No. of patient drop-out from study (per site)	
退出原因 Reasons for drop-out：	

研究方案/主要研究者有否改變？(如有，請提供詳情) Any changes for study protocol/principal investigator? (If yes please give details)
報告期內所作修訂的撮要 (如有，請提供) Summary of amendments during report period (if any)

嚴重不良事故的撮要 (如有，請提供) Summary of Serious Adverse Events (if any)
嚴重不良事故有否影響研究？有何影響及採取的行動？ Does SAE affect the study? How and what action has been taken?
針對研究所提出的投訴撮要 (如有，請提供) Summary of complaints about the study (if any)

近期研究結果的撮要 (特別是關於研究所涉風險的資料) Summary of recent findings (especially information about risks associated with the research)

試驗藥物的用藥紀錄 (如多於 1 種試驗藥物，請另頁填寫)：

Record of usage of the investigational product (If more than 1 investigational product, please use a separate sheet):

試驗藥物名稱 Name of investigational product			
供應單位及地址 Name and address of supplier			
收貨數量 Quantity received		日期 Date	
使用後的餘額 Remaining quantity after use		日期 Date	

研究進度 Progress of study

- ☐ 按計劃進行 According to Plan
- ☐ 研究期延長 (原因_____)
  Extend study period (Reason_____)
- ☐ 中途結束 (原因_____)
  Premature termination (Reason_____)

研究者姓名 Name of Investigator：	簽署 Signature：
職位 Posting：	日期 Date：
機構名稱及地址 Name and Address of Organization：	

如空位不敷填寫，請另頁詳列有關資料，並在有關部份註明。負責人須在該頁上註明其姓名和簽署，然後將附頁釘夾在此報告；如對填寫以上資料有任何查詢，可於辦公時間致電衞生署中醫藥規管辦公室查詢，電話：3904 9130。
If there is insufficient space, please use a separate sheet and indicate accordingly in the relevant part of the Report. The responsible person should write his name and sign on the attached sheet, and attach it to the report; if you have any enquiries when filling in the above information, please contact the Chinese Medicine Regulatory Office of the Department of Health at 3904 9130.

收件日期: 檔案編號:

臨床試驗最後報告

Clinical Trial Final Report

報告期 Report period	至 to		
本報告日期 Date of this report (dd-mm-yyyy)：			
臨床證驗及藥物測試證明書編號 Number of Certificate for Clinical Trial and Medicinal Test :			
方案編號 Protocol no.：			
方案標題 Protocol title：			
開始日期 Start date：	日Day	月Month	年Year
結束日期 End date：	日Day	月Month	年Year

目標病人數目(方案所載) Target no. of patient (as stated in protocol)	
擬招募病人數目(每個地點) No. of patient intended to recruit (per site)	
已招募病人數目(每個地點) No. of patient recruited (per site)	
完成試驗的病人數目(每個地點) No. of patient completed the trial (per site)	
退出試驗的病人數目(每個地點) No. of patient drop-out from study (per site)	
退出原因 Reasons for drop-out：	

嚴重不良事故的撮要 (如有，請提供) Summary of Serious Adverse Events (if any)
嚴重不良事故有否影響研究？有何影響及採取的行動？ Does SAE affect the study? How and what action has been taken?
針對研究所提出的投訴撮要 (如有，請提供) Summary of complaints about the study (if any)

研究結果的撮要 Summary of study outcome：

試驗藥物的用藥紀錄 (如多於 1 種試驗藥物，請另頁填寫)：

Record of usage of the investigational product (If more than 1 investigational product, please use a separate sheet):

試驗藥物名稱 Name of investigational product			
供應單位及地址 Name and address of supplier			
收貨數量 Quantity received		日期 Date	
使用後的餘額 Remaining quantity after use		日期 Date	
剩餘試驗藥物的處理方法 Handling of the remaining investigational product			

研究進度 Progress of study

- ☐ 按計劃進行 According to Plan
- ☐ 研究期延長 (原因_____)

  Extend study period (Reason_____)
- ☐ 中途結束 (原因_____)

  Premature termination (Reason_____)

研究者姓名 Name of Investigator：	簽署 Signature：
職位 Posting：	日期 Date：
機構名稱及地址 Name and Address of Organization：	

如空位不敷填寫，請另頁詳列有關資料，並在有關部份註明。負責人須在該頁上註明其姓名和簽署，然後將附頁釘夾在此報告；如對填寫以上資料有任何查詢，可於辦公時間致電衞生署中醫藥規管辦公室查詢，電話：3904 9130。

If there is insufficient space, please use a separate sheet and indicate accordingly in the relevant part of the Report. The responsible person should write his name and sign on the attached sheet, and attach it to the report; if you have any enquiries when filling in the above information, please contact the Chinese Medicine Regulatory Office of the Department of Health at 3904 9130.

Figure 1

Flowchart on Processing of Applications for Variation of Information made by Holders of the Certificate for Clinical Trial and Medicinal Test ("the Certificate")