1.目的 Purpose

規範人委會處理及審查計畫變更案之流程。

To establish regulations for the IRB to handle and review the amendments.

2. 適用範圍 Scope

適用於已通過審查之研究計畫案，變更案須經人委會審查通過後方能執行。

It is applicable to approved study protocols. Amendments can only be implemented after the approval of the IRB.

3.參考文件 References

3.1藥品優良臨床試驗準則（2014年10月）

Guidelines of Good Clinical Practice (October 2014)

3.2人體研究法（2011年12月）

Human Subject Research Act (December 2011)

3.3World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.

3.4 International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.

3.5 Code of Federal Regulation (CFR), 21 §56.110, The United States of America, 1998

4.名詞定義 Terminology

4.1 變更案文件：研究進行中之計畫案，因特定因素更改執行內容或相關資料時，所需檢送之申請表、修正文件及修正前後對照表。

Amendments: refer to ongoing study protocols that require amendments on the content or relevant information. It is required to submit the application form,

amendments and the comparison table before and after amendments.

4.2 行政變更：當計畫案之修改內容，不影響受試者權益者，例如僅新增試驗場所、新增/變更共同主持人或協同主持人、聯絡方式改變等。

Administrative amendment: The amendments do not affect the rights of the subjects, e.g. add/change co-investigators or sub-investigators, contact information, etc.

4.3 實質變更：當計畫案之修改內容涉及計畫之執行內容，會影響受試者權益者，例如試驗相關程序異動/變更、研究相關文件的增減、受試者所承受之風險/利益改變等。

Substantial amendment: The amendments involve in study implementation that may affect the rights of the subject, e.g. the changes/amendments on study-related procedures, addition/reduction of study-related documents, changes in the risks/benefits levels of the subjects, etc.

4.4 試驗核准期間 (Approval period): 人委會審查會議核准此研究計畫案可執行的期限。

Approval period: The study implementation duration approved by the IRB.

4.5 研究期間 (Research time frame): 該研究計畫案預計執行的期間。

Research time frame: The expected study implementation time frame.

5.作業內容 Scope of operation

5.1 流程 Process

程序 Procedure	**權責 Rights and responsibilities**	**相關文件 Related documents**
送交申請資料 Submit the application	計畫主持人/申請人 Principal	依送審文件清單 Checklist of files for

	Investigator/Applicant	submission
確認送審文件 Verify the submitted files	行政人員 Administrative staff	依送審文件清單 Checklist of files for submission
審查 Review	原初審委員 Original reviewers	送審資料 Submitted files for review
審查會議 Review Meeting	人委會 IRB	會議議程/紀錄 Meeting agenda/minutes
製作核准文件 Prepare approved files 歸檔 Archiving	行政人員 Administrative staff	公文 Official letter 變更同意書 Approval for amendments

5.2 職責 Responsibilities

5.2.1 主任委員：指派委員/專家審查。

Committee director: The person who can appoint IRB members/experts for review.

5.2.2 審查委員/專家：於期限內完成審查程序，並將審查意見送回人委會。

Reviewers/Experts: shall complete review procedures and send back the review comments to the Administrative staff.

5.2.3 行政人員：受理申請案件、申請資料建檔、彙整審查意見至人委會會議審查、審查會決議通知計畫主持人。

Administrative staff: receive applications, document study protocols, summarize review comments and report to the IRB meeting for further review, and notify review results to the Principal Investigator.

5.3 細則 Rules

5.3.1 變更案申請

Apply for amendments

5.3.1.1 申請人至 PTMS 系統填寫變更案申請表(附件一)。

The applicant shall go to the PTMS system to submit an amendment application form (Attachment 1).

A.行政變更包括：

Administrative amendment consists of:

(A)試驗/研究相關人員異動/新增(共同/協同主持人、研究護理師/研究助理)。

Trial/study personnel changes/addition (co-/sub-investigators, research nurse/assistant).

(B)改變文字敘述方式，但內文意義不變。

Changes in word descriptions but the meaning has remained unchanged.

(C)相關聯絡資訊異動/變更(24 小時連絡人員、聯絡窗口)。

Changes/amendments on contact information (24-hr contact person, contact pathway).

(D)其他對受試者之風險/利益幾乎無影響之變更。

Amendments that do not affect the risks/benefits of the subjects.

B.實質變更包括：

Substantial amendments consist of:

(A)對受試者之風險/利益有所影響(例如：副作用、劑量、療效等資訊變更)。

Amendments that affect the risks/benefits levels of the subjects (e.g. information changes like side effects, doses, efficacy, etc.)

(B)試驗/研究相關程序、方式的異動/變更(例如：問卷、檢查等程序的異動等)。

Changes/amendments on trial/study-related procedures and approaches (e.g. procedural changes like questionnaire, examinations, etc.)

(C)試驗/研究相關文件的增減。

Add/delete trial/study-related files.

(D)其他可能影響受試者安全或權益需實質審查者。

Others that may affect the safety or rights of the subjects and thus require substantial review.

5.3.3.2 計畫主持人依據下列項目評估是否會增加受試者風險。

The Principal Investigator will evaluate whether the risks of the subjects will be increased by changing the following items:

A.一般審查

Regular review

(A)新增或刪除治療/檢查。

Add or delete treatments/examinations.

(B)劑量減少或增加。

Decrease or increase dose.

(C)任何納入/排除條件的改變。

Changes in inclusion/exclusion criteria.

(D)用藥方法的改變，例如口服改成靜脈注射。

Changes in drug administration, e.g. from oral intake to IV injection.

(E)受試者人數大幅度的改變：

Significant changes in subject sample size:

a.原收案人數 20 人以下，變更人數≧5 人。

If the original sample size is under 20 persons, changes ≧5 persons.

b.原收案人數 20 人以上，變更人數≧20 %。

If the original sample size is above 20 persons, changes ≧20 %.

(H)緊急事件：為即時保護受試者，避免受試者傷害而改變計畫書程序時，計畫主持人應於事件獲知後 7日內將變更之內容及其原因依不遵從事件(含試驗偏差、違規)通報人委會，並提出變更案審查；經主管機關核准進行之臨床試驗，應同時將變更案提交主管機關。

Emergencies: To promptly protect the subjects and prevent the subjects from damages and change the study protocol, the study Principal Investigator shall report the amendments and

the reasons to the IRB as noncompliance (including study deviations, violations) within 7 days after being notified about the events and apply for amendment review. For the implementation of the clinical studies approved by the competent authorities, the application of amendments shall be submitted to the competent authorities at the same time.

B.簡易審查

Expedited review

(A)受試者人數小幅度的改變：

Minor changes in subject sample size:

a.原收案人數 20 人以下，變更人數＜5 人。

If the original sample size is under 20 persons, changes ＜5 persons.

b.原收案人數 20 人以上，變更人數＜20 %。

If the original sample size is above 20 persons, changes ＜20 %.

(B)行政事務變更 （如：計畫書聯絡人地址、電話）

Administrative affair amendments (e.g. the address and TEL of the contact person in the study protocol)

(C)改善文句通順程度或說明更詳細

Change the wordings/sentences to increase the fluency or elaborate the contents more detailed

(D)研究期間展延：僅限於時間的展延，不含其他變更。需說明展延期間及原因。

Study period extension: Limit to time frame extension, other amendments are not included. The period of extension and reasons of applying for extension shall be explained.

5.3.3.3 行政變更：若計畫僅新增試驗場所、新增/變更共同主持人或協同主持人、聯絡方式改變等，不影響受試者權益之行政變更，行政人員核對申請資料內容無誤後，列入審查會議中決議即可。

Administrative amendments: if the study only undergoes administrative amendments that do not affect the rights of the subjects such as add new trial sites, add/change co-investigators or sub-investigators, change contact information, the amendments will be scheduled in the review meeting for resolutions after the Administrative staff have verified the accuracy of the application files.

5.3.3.4 工作人員將變更案，送交原審查委員審查。原主審委員因故無法審查時，由主任委員以變更案分案表另外指派審查委員審查。若執行秘書曾任醫療委員，主任委員得授權執行秘書分案。

The staffs shall send the amendments to the original reviewers for review. If the original reviewers are unable to review due to certain reasons, the chairperson shall appoint other reviewers for amendment review based on the case allocation form. If the executive secretary

were medical members, the chairperson may authorize the executive secretary to allocate the review of amendments.

5.3.2 審查 Review

5.3.2.1 審查委員使用變更案審查意見表(一般審查/簡易審查) (附件二)進行初審審查，提交行政人員彙整，並勾選是否邀請諮詢專家或受試者(團體)代表列席或提供書面資料。審查期限為 5 個工作日。若委員發現遺漏審查資料，則應告知行政人員。

The reviewers will use the Amendment Review Comment Forms (regular review/expedited review) (Attachment 2) to perform initial review, submit to the Administrative staff for summary, and decide whether the invitation of consultant experts or subject (group) representatives to attend the meeting for provide written documents are required. The review shall be completed within 5 working days. If the reviewer has found that he/she has missed reviewing some materials, he/she shall notify the Administrative staff.

5.3.2.2 若有審查委員認為不符合原申請狀態，行政人員發通知信通知計畫主持人，告知其原因及更改審查狀態。

If any reviewers have considered the case does not meet the original applications status, the Administrative staff will issue a letter to notify the Principal Investigator and inform the Principal Investigator about the reasons and ask the Principal Investigator to apply for another type of review.

5.3.2.3 審查重點：

Review items:

A.變更之內容及原因。

The contents and reasons of amendments

B.變更後受試者之風險是否增加？

Have the risks of the subjects been increased after amendments?

C.變更後是否影響受試者之權益？

Will the subject's rights be affected after amendments?

D.變更後是否有新訊息需提供給受試者？

Is there any new information needed to be provided to the subject after amendments?

E.是否需重新簽署受試者同意書？

Will the subject ICF be signed again?

5.3.2.5 必須重新簽署受試者同意書：

The subject ICF shall be signed again:

A.變更計畫以致受試者風險增加

Amend the study protocol and lead to increased subject's risks

B.發生非預期事件，而產生新的風險

The occurrence of UP and thus result in new risks

C.影響受試者權益之重大事件

Major events that will affect the rights of the subjects

D.新增治療或檢查

New addition of treatments or examinations

5.3.3 審查會議

Review meeting

5.3.3.1 行政人員彙整委員初審審查意見，排入就近日期委員會議審議。

The Administrative staff will summarize the initial review comments from the reviewers and schedule the application into latest IRB Meeting for discussion.

5.3.3.2 會議審議結果得為下列之決定：

The meeting results may be as follows:

A.【核准】：行政人員以變更案決議通知 (附件三)通知申請人/ 計畫主持人，並製作新案/變更案/期中報告同意證明書 (附件四) ，送交主任委員簽核，行政人員應於會議結束後 10 個工作日內，將同意書掃描後 E-Mail 給申請人/ 計畫主持人，正本由行政人員歸檔存查。

[Approved]: the Administrative staff will use Notifications of Amendment Resolutions (Attachment 3) to notify the Applicant/ Principal Investigator, establish New Applications/Amendment/Continuing Review Consent Form (Attachment 4), and send to the Committee director for signature and approval. The Administrative staff shall scan the consent form and E-Mail to the applicant/ Principal Investigator within 10 working days after the termination of the IRB meeting. The original files shall be retained by the Administrative staff for reference and archiving.

B.【修正後複審 】：申請人/計畫主持人就初審審查意見修正後，依 SOP 2.7 複審案標準作業程序進行複審。

[Secondary review after amendment]: after the Applicant/ Principal Investigator has amended the files based on the initial review comments, the amendments will be sent for secondary review in accordance with SOP 2.7 for Secondary Review.

C.【修正後入會】：審查委員認為有實質改變、要求或需要更多的信息及涉及核准條件的其他議題時，行政人員應通知計畫主持人修正，並將修正後之變更案交由最近一次之審查會議審查。

[Resubmission after amendment]: if the reviewers believe that the substantial amendment are required, or require more information, or other topics have involved in approval criteria, the administrative staff shall inform the Principal Investigator to amend the files, and send the amendments to the latest review meeting for review.

D.【不核准】行政人員應於會議結束後 10 個工作日內，將會議審議結果，以審議結果通知表通知計畫主持人，並詳細說明不核准理由。申請人/計畫主持人如需申覆，應於 14 個工作日內以書面資料提出。若未於 14 個工作日內提出申覆，則依原審議結果辦理。

[Not approved]: the administrative staff shall inform the Principal Investigator about the review results within 10 working days after the completion of the meeting, and describe the reasons of not

being approved. If the Applicant/ Principal Investigator intends to re-apply, he/she shall submit a written application within 14 working days. If they fail to re-apply within 14 working days, relevant matters will be processed in accordance with the original review results.

5.3.3.3 變更案同意書核准效期計算

The calculation of valid duration of the amendment approval

A.核准期間(Approval period)：從核准日(審查通過日)至最近一次之新案/持續審查案同意書之迄日。

Approval period: from the date of approval (the date that the review of the amendment has been granted) to the last date of the latest new application/continuing review approval.

B.期中報告及研究期間展延核准者，試驗核准期間將依據申請年限給予展延(至多 1 年)。

For those have been granted for interim report and study period extension, the approved study duration will be extended (up to 1 year) based on the applied time frame.

C.研究期間展延：一年期之研究案或多年期研究案之最後一年，因故需要延長研究期間 (Research time frame)，可同步於繳交期中報告時提出，或須於核准迄日 2 個月前提出 (應繳期中報告迄日)，迄日 2 個月後只能先提期中報告再展延。研究期間展延必須等期中報告審查通過後方可給予核准。

Extension of study period: For the one-year study or the last year

of the multiple-year study, if the research time frame is required to be extended due to certain reasons, the application for study extension can be applied at the same time with the submission of interim report. It can also be applied 2 months prior to the expiration date of the approved valid duration (the date to submit required interim report). Once the approved valid duration has expired, the Principal Investigator can only submit the interim report first and then apply for study extension 2 months after the expiration date of the approved valid duration. During the study period, the application for study extension can only be granted after the interim report has been approved.

D.試驗有效期間(approval period)已屆滿，所有的研究活動須停止。
When the approval period has been expired, all research activities must be stopped.

5.3.4 文件歸檔：依標準作業程序（SOP 6.1）進行。

File archiving shall be processed in accordance with SOP 6.1.

6.附件 Attachment

6.1 附件一(KMUH/IRB/AF/2.9-01/11.0) 變更案申請表

Attachment 1 (KMUH/IRB/AF/2.9-01/11.0) Amendment Application Form

6.2 附件二(KMUH/IRB/AF/2.9-02/11.0) 變更案初審審查意見表

Attachment 2 (KMUH/IRB/AF/2.9-02/11.0) Amendments Initial Review Comment Form

6.3 附件三(KMUH/IRB/AF/2.9-03/11.0) 變更案決議通知

Attachment 3 (KMUH/IRB/AF/2.9-03/11.0) Notifications of Amendment Resolutions

6.4 附件四(KMUH/IRB/AF/2.9-04/11.0) 人體研究新案/變更案/期中報告同意證明書

Attachment 4 (KMUH/IRB/AF/2.9-04/11.0) Approval of Clinical Trials/Research (New Applications/Amendments/Interim Reports)