1.目的 Purpose

提供人委會對於已通過的計畫案之追蹤審查相關作業指引，以確保受試者在研究過程的安全、權益及福祉。

To provide the IRB with continuing, review-related operational guidelines for approved protocol to ensure the safety, rights and welfare of the subjects during study period.

2. 適用範圍 Scope

適用在任何人體相關的研究計畫案之追蹤審查事宜，包含期中報告、嚴重不良事件、未預期事件或實地訪視監測。

It is applicable to the follow-up review of any human-related study protocol, including interim reports, Serious Adverse Event (SAE), Unanticipated Problems (UP) or field inspection/monitoring.

3.參考文件 References

3.1 藥品優良臨床試驗準則(2015 年 10 月)

Guidelines of Good Clinical Practice (October 2015)

3.2 人體研究法（2011 年 12 月）

Human Subject Research Act (December 2011)

3.3 World 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.

4.名詞定義 Terminology

4.1 期中報告：已核准的研究計畫案於未結案前之執行進度與狀況報告。

Interim report: refers to the execution progress and status report of approved

study protocol before closure.

4.2嚴重不良事件：因試驗致發生下列反應者，如：

SAE refers to studies lead to the following reactions, including:

A.死亡：如病患死亡被認為係不良事件之直接結果。

Death: the patient's death is considered to be the direct results of AE.

B.危及生命：如病患於發生不良事件時有死亡危險，或如繼續使用試驗產品可能造成病患死亡。(例如：心臟節律器功能喪失、胃腸道出血、骨髓功能抑制、輸液幫浦功能異常造成藥物劑量過量等。)

Life-threatening: the patient has risks of death due to AE, or may be dead if continuing using investigational products (e.g. pacemaker dysfunction, GI bleeding, bone marrow inhibition, infusion pump dysfunction-caused overdose, etc.)

C.導致病人住院或延長病人住院時間：如因不良事件發生導致病患需住院或延長住院時間。(例如：過敏性反應；偽膜性結腸炎；出血導致住院或延長住院時間等。)

Hospitalization of prolonged hospitalization: AE-caused patient hospitalization or prolonged hospitalization (e.g. allergic reaction, pseudomembranous colitis, hospitalization or prolonged hospitalization caused by bleeding, etc.)

D.永久性殘疾：如不良事件對病患身體功能/結構、身體活動或生命品質，造成嚴重性、永久性的改變、損害或傷害。(例如：因藥物引起過度凝集之腦血管意外、中毒、周邊神經病變等。)

Permanent disability: AE-caused serious and permanent changes, damages or harm to patient's physical function/structure, physical activity or quality of life. (e.g. cerebrovascular accident caused by drug-induced excessive agglutination,

poisoning, peripheral neuropathy, etc.)

E. 導致胎兒先天性畸形：如於懷孕前或懷孕期間暴露於藥品導致胎嬰兒不良結果。(例如：母親懷孕時服用 diethylstilbestrol 造成女性胎兒罹患子宮頸癌、thalidomide 造成胎兒畸形等。)

Cause congenital fetal deformity: drug exposure before or during pregnancy and result in adverse results to the fetus (e.g. pregnant women taking diethylstilbestrol and result in female fetus suffering from cervical cancer, thalidomide-induced fetus deformity, etc.)

F. 其他可能導致永久性傷害需作處置者：懷疑因使用藥品造成需要內科或外科介入治療以防止病患永久性失能或傷害。(例如：Acetaminophen 劑量過量導致肝毒性，需以 acetylcysteine 治療以避免永久傷害；放射線設備造成之灼傷，需以藥物治 療；螺絲破損需更換以避免長骨骨折之接合不良等。)

Other events that may cause permanent damage and thus require corresponding handling: suspect that the use of drugs may need internal or surgical intervention to prevent patients from being dysfunctional or damaged permanently (e.g. Acetaminophen overdose may lead to hepatotoxicity and requires the treatment of acetylcysteine to prevent permanent damages. Burn injuries caused by radiation equipment and require drug therapy. The replacement of screws is required due to screw damages to prevent long bone fracture from malunion, etc.)

4.3 未預期事件：符合以下 3 個條件:

Unanticipated Problems (UP): has met the following three conditions:

A. 非預期 (unexpected): 記載於計畫書(study protocol)/ 主持人手冊(investigator brochure)/ 藥品仿單(product monograph)/受試者同意書(informed consent form)之不良反應稱之為預期, 未記載於上述資料的事件、或發生率嚴重性超過預期之情 形,則稱之為非預期

Unexpected: the adverse reactions documents in the study protocol/investigator brochure/product monograph/informed consent form are called expected AEs. Those events that are not listed in the above documents or the severity of the event has exceeded the expected level is called unexpected adverse events (AEs).

B. 可能相關

Potentially relevant

C. 對受試者及其他研究人員的傷害(身體、心理、經濟及社會層次)超過已知的風險

The damages (physical, psychological, economic and social levels) to the subjects and other research personnel have exceeded known risks.

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 Investigator/Applicant	依送審資料清單 Checklist of files for review
確認送審文件內容 Verify the contents of submitted documents	行政人員 Administrative staff	依送審資料清單 Checklist of files for review
指派審查委員/專家	主任委員	分案表

Appoint reviewers/experts	Committee director	List of case classification
審查 Review	審查委員/專家 Reviewer/Expert	送審資料 Files for review
審查會議 Review Meeting	人委會 IRB	議程資料 Meeting agenda
通知審查結果 Notify review results	行政人員 Administrative staff	同意書、通知文件 Consent form, Notification
歸檔 Archiving	行政人員 Administrative staff	相關資料 Related documents

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,並將審查意見送回行政人員。

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、計畫案件建檔、審查意見彙整至人委會會議審查、會議結果通知計畫主持人、相關文件歸檔。

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

5.2.4 人委會：發現異常事件時，得啟動實地訪視監測程序

If the IRB has uncovered aberrant events, field inspections and surveillance procedures shall be activated.

5.3 細則 Rules

5.3.1 期中報告通知：依試驗計畫特性（含多年期計畫案），訂定追蹤審查之頻率：每年一次、每 6 個月一次或每 3 個月一次。

Notification of interim report: the frequency of follow-up review on interim report can be set based on the property of the study protocol (including multi-year protocols): Once annually, once every 6 months or once every 3 months.

5.3.1.1 期中報告應繳交日依追蹤審查之頻率訂定。最後一次期中報告應繳交日為核准有效期限 2 個月前，若該研究已完成，則請直接繳交結案報告。

The required submission date is set based on the frequency of follow-up review. The required submission date of the last interim report is 2 months before the approved valid duration. If the study has been completed, please submit the closure report instead.

5.3.1.2 人委會通知繳交期中報告：

IRB notifying about submitting interim report:

A. 第一次通知：自應繳交日算起，前 4 週。

The 1st notification: 4 weeks prior to the required submission date.

B. 第二次通知：自應繳交日算起，前 2 週。

The 2nd notification: 2 weeks prior to the required submission date.

C. 第三次通知：應繳交日當日。

The 3rd notification: the required submission date.

D. 第四次通知：超過應繳交日4週。

The 4th notification: 4weeks after the required submission date.

E. 第五次通知：超過核准有效期限。

The 5th notification: exceeded the approved valid duration.

5.3.1.3 超過應繳交日相關處理

Relevant handling when exceeding the required submission date

A. 超過應繳交日4週，提人委會討論暫停納入新受試者。

If exceeded 4 weeks, the application shall be reported to the IRB or suspend its new subject enrollment.

B. 超過核准有效期限，人委會決議研究計畫暫停或永久終止，並得啟動實地訪視監測程序。

If exceed approved valid duration, the IRB may decide to suspend or permanently terminate the study and activate field inspection and surveillance procedures.

5.3.1.4 期中報告於核准期間迄日仍未通過審查者

The interim report hasn't been approved on the last date of the approved valid duration.

A. 試驗有效期間已屆所有的研究活動須停止。

All research activities must stop since the valid duration of the study is expired.

B. 在安全性考量下無法立即停止試驗者，計畫主持人需向本會提出說明，並檢附需繼續執行之受試者清單，經主任委員同意後，該等受試者方可繼續執行。

For the studies cannot be stopped immediately due to safety reasons, the Principal Investigator is required to submit a description and attach a subject list including subjects who need to continue participating in the study. Those subjects can only continue participation until the application has been approved by the committee director.

C. 人委會得拒絕計畫主持人申請新案(含審查中新案),直到該案的期中報告審查結束。

The IRB has the right to refuse the Principal Investigator applying for new studies (including new application that are currently under review) until the review of the interim report has been completed.

5.3.2 期中報告繳交

The submission of interim report

5.3.2.1計畫主持人或試驗委託者應於人體試驗同意證明書有效期限到期前 2 個月，依規定檢附相關文件，提出期中報告。

The Principal Investigator or Sponsor is required to attach relevant documents and submit an interim report 2 months prior to the expiration date noted in the Certificate of Approval issued by the IRB.

5.3.2.2 行政人員於收到期中報告，依送審文件清單確認內容。

The administrative staff shall verify all the files based on the checklist of files for review once they have received the interim report.

5.3.2.3 檢附之受試者同意書須提供第一頁基本資料、簽名頁及需受試者勾選之頁面影本。

The attached subject Informed Consent Form (ICF) must contain basic data on the 1st page, signature page, and page copies that require subject's selection.

A.收案人數 30 份以下，全部檢附。

If the sample size is 30 or less, all files shall attach the above information.

B.收案人數 31 份以上、100 份以下：行政人員代抽查 30 份予審查者審查，若有問題全部審查。

If the sample size is between 31~100, the administrative staff will randomly select 30 applications and send them to the reviewer for review. If any problems were uncovered, all applications shall be reviewed.

C.收案人數 100 份以上：第 1 次行政人員代抽查 30 份予審查者審查，若有問題再抽審 30 份，還是有問題全部審查。

If sample size is above 100, the administrative staff will primarily select 30 applications and send them to the reviewer for review. If any problems were uncovered, another 30 application will be reviewed. If problems are still uncovered, all applications shall be reviewed.

D.正本由計畫主持人自行保管，人委會及主管機關得隨時調閱。

The Principal Investigator shall retain the original copy for the IRB and competent authorities to review at any time.

5.3.2.4 執行秘書須依受試者同意書稽核表(附件一)核對受試者同意書是否正確簽署。核對期限為 7 個工作日。

The executive secretary shall verify whether the subject Informed Consent Form (Attachment 1) has been signed properly based on the requirements stated in the subject Informed Consent Form audition form. The verification duration is 7 working days.

5.3.3 期中報告審查

Review of interim report

5.3.3.1 送交原初審委員/專家審查，時限為 7 個工作日。依期中報告審查意見表 (附件二)審查重點：

The time limit of sending the application to the original reviewers/experts for review is 7 working days. The review focuses of the Interim Report Review Comment Form (Attachment 2) are as follows:

A. 期中報告表(附件三)

Interim Report Form (Attachment 3)

B. 期中報告個案收案表 (附件四)

Case Report Form (Attachment 4)

C. 受試者同意書第一頁及簽名頁影本

The 1st page of subject Informed Consent Form and the copy of signature page

D. 不良事件是否依規定通報

Whether the AE is reported following the rules

E. 評估本次期中報告是否有發現未經 IRB 核准而變更計畫之事件

To evaluate whether there are any amendments without IRB approval in the interim report

F. 評估本次期中報告是否有任何新的調查結果，會影響受試者參與意願

To evaluate whether there are any new investigational results that may affect the willingness of the subjects to participate in the study

G. 評估本次期中報告是否有任何新的資訊，須提供給受試者知道

To evaluate whether there are any new information that must be provided to the subjects

5.3.3.2人委會審查會議，將期中報告審查結果送交委員會決議，採共識決決議。會議後7個工作日以電子郵件通知計畫主持人及試驗委託者本案之會議後決議等相關資訊。審查結果為

The IRB meeting will send the interim report review results to the Committee for making resolutions. 7 working days after the meeting, the IRB will notify the Principal Investigator and Sponsor through e-mail about meeting resolutions and relevant information. The review results may be as follows:

A.【核准】：人委會出具「人體試驗/研究期中報告同意證明書」（附件五）。查驗登記用臨床試驗計畫案之期中報告

審查通過後，人委會函送一份至衛福部審核。

[Approved]: the IRB will issue a "Certificate of Approval for Human Trial/Study Interim Report" (Attachment 5). After the review of interim report of clinical trials for registration has been approved, the IRB will issue an official letter to Ministry of Health and Welfare for review.

B.【修正後複審】：依審查會會議意見修改，重新送審。

[Secondary review after amendment]: the Principal Investigator shall amend the study protocol based on the review comments and resubmit the amended files for secondary review.

C.【不核准】：人委會得暫停計畫案進行，請計畫主持人進行說明，並得啟動實地訪視監測。

[Not approved]: the IRB may suspend the study protocol, request the Principal Investigator for descriptions and activate field inspection and surveillance procedures.

5.3.4 嚴重不良事件(SAE)/未預期事件(UP)的通報及審查，依標準作業流程(SOP 3.3)進行。若計畫案發生嚴重不良事件(SAE)/未預期事件(UP)時，得經人委會審查會議決議要求計畫主持人或試驗委託者提前繳交期中報告。

The report and review of SAE/UP shall be in accordance with SOP 3.3. If any SAE/UP occurs during the study, according to the IRB review resolution, the IRB can request Principal Investigator or Sponsor to submit interim reports in advance.

5.3.5 文件歸檔依標準作業流程(SOP 6.1)進行。

File archiving shall be in accordance with SOP 6.1.

6.附件 Attachment

6.1 附件一(KMUH/IRB/AF/2.8-01/11.0) 受試者同意書稽核表

Attachment 1 (KMUH/IRB/AF/2.8-01/11.0) Subject ICF Audition Form

6.2 附件二(KMUH/IRB/AF/2.8-02/11.0) 期中報告審查意見表

Attachment 2 (KMUH/IRB/AF/2.8-02/11.0) Interim Report Review Comment Form

6.3 附件三(KMUH/IRB/AF/2.8-03/11.0) 期中報告表

Attachment 3 (KMUH/IRB/AF/2.8-03/11.0) Interim Report Form

6.4 附件四(KMUH/IRB/AF/2.8-04/11.0) 期中報告個案收案表

Attachment 4 (KMUH/IRB/AF/2.8-04/11.0) Interim Report Case Report Form

6.5 附件五(KMUH/IRB/AF/2.8-04/11.0) 人體研究新案/變更案/期中報告同意證明書

Attachment 5 (KMUH/IRB/AF/2.8-04/11.0) Approval of Clinical Trials/Research (New Applications/Amendments/Interim Reports)