Guidelines

by

Human Experimentation Committee (HEC)

Version 4.3

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Preface

Research Institute for Health Sciences (RIHES), Chiang Mai University (CMU) conducts research in health-related disciplines that will address the country's public health issues, particularly in the Northern region. The research projects conducted by RIHES receive funding from domestic and overseas bodies and most of them have to be conducted in humans. That is, they are research that involves human subjects, including bodies, human specimens, medical records, test results, as well as psychological studies. Conducting human subject research must adhere to international ethical principles and Thai social and cultural values. RIHES has appointed a research ethics committee called the Human Experimentation Committee (HEC) which is responsible for giving approval to human research protocols conducted and/or co-conducted by RIHES; protocols by another institution that are requested to be conducted at RIHES; and protocols by other CMU organisations that do not have an ethics committee or equivalent, or have an ethics committee but have filed for additional review regarding issues within HEC's areas of expertise.

The Working Party for Establishing the Standard Procedure for the Human Experimentation Committee, RIHES has created these guidelines on the approval process and research protocol preparation to help investigators meet all document requirements upon submission. These guidelines have been revised from the 2005, 2008, 2015, and 2021 editions. It is hoped that they will be of use to investigators as a research manual.

The Working Party for Establishing the Standard Procedure
for the Human Experimentation Committee
February 2023

Table of Contents

Chapter 1
Introduction

1.1 Background of the Human Experimentation Committee, Research Institute for Health Sciences (RIHES)

The Research Institute for Health Sciences (RIHES), Chiang Mai University was founded in 1978 as the centre of support for conducting research in health-related fields from biomedical, clinical, epidemiological to behavioural research, focusing on public health issues in Northern Thailand and drawing implications that will address public health concerns in other parts of Thailand and the world with similar socio-economic conditions. Most research conducted by RIHES involves human experimentation and, therefore, the Human Experimentation Committee (HEC) has been established to protect the rights, safety and well-being of participants and participating communities.

1.2 Assurance

At present, the Institute receives research funding from domestic and international bodies, among which is the National Institute of Health (NIH), which is a US federal agency. Every institution that conducts human subject research and receives funding from the US federal government must follow the Code of Federal Regulations, Title 45, Part 46 on Protection of Human Subjects, 45 CFR 46 and has assurance in writing with the US federal government. This means that to comply with the US federal law the Institute has registered its research ethics committee and filed for Federalwide Assurance (FWA) for the Protection of Human Subjects for International (Non-US) Institute approved by the US Department of Health and Human Services (DHHS). The details are as follows.

Registration Number: IRB00003605

Assurance Name: Chiang Mai U, Rsch Inst Hlth Sci IRB #1

Assurance Number: FWA 00005355

The Institute must follow the regulations for the protection of human subjects in research in the Code of Federal Regulations at 45 CFR 46, as stated above. The Office for Human Research Protections (OHRP), DHHS is responsible for operations related to FWA to ensure that participants of research are treated under the Code of Federal Regulations at 45 CFR 46. Strict protection shall be provided and the research ethics committee shall receive assessment, as well as constant learning opportunities.

Moreover, HEC has been certified by WHO-TDR-SIDCER (The Strategic Initiative for Developing Capacity for Ethical Reviewer) in partnership with FERCAP (Forum for Ethical Research Committees in Asia and Western Pacific) in 2008, 2011, 2015 and 2019. Inspection visits and performance assessments are conducted consistently to provide assurance for funding bodies, researchers, and journals.

1.3 RIHES Responsibilities

The RIHES's responsibilities are as follows:

1) Appoint an HEC to review scientific protocols and research ethics, and approve protocols, as well as support HEC's operation to ensure fairness and independence from interference;
2) Protect the rights and welfare of the subjects by requiring the investigators to present their human protocols to HEC for approval – the investigators may only begin their research on the approval date as stated in the Certificate of Approval. Any amendment to the protocol must be filed for approval;
3) Provide HEC with sufficient resources such as meeting locations, document storage, administrative personnel, and office equipment;
4) Encourage HEC to participate in research ethics training for improved capacity in research approval; and
5) Promote cooperation between local, national, and regional ethics committees to create a network of information exchange.

1.4 Ethics Committee Responsibilities

HEC of RIHES is appointed to protect the rights, safety, and welfare of human subjects. HEC's responsibilities and authorities are as follows:

1) Review protocols conducted or co-conducted by RIHES and protocols conducted by other organisations that have requested to conduct the research at RIHES, on the basis of rights protection and harm prevention; and make a decision to approve, approve with revision or reject;
2) Review human research protocols conducted by CMU organisations that do not have an ethics committee or equivalent, or have an ethics committee but have filed for additional review regarding issues within HEC's areas of expertise; and make a decision to approve, approve with revision or reject;

3) Monitor the progress of approved protocols until completion by reviewing the Progress Report at least once a year depending on the risk to ensure that the ongoing research is in line with the proposed methodology and reports new findings that are of benefit to the subjects; and make a decision to extend the research period, temporarily suspend or terminate approval;
4) Review amendment proposals for approved protocols; and make a decision to approve, approve with revision or reject;
5) Review reports of serious adverse events, unexpected and relevant events, deviations or violations of the approved protocol, non-compliances of regulations, or violations of research ethics; and make a decision to temporarily suspend or terminate approval if it is deemed that further harm to participants will arise should the research continues;
6) Appoint independent consultants who may provide specialised assistance to HEC such as disease or methodology specialists, or community or patient representatives;
7) Conduct field visits at research locations and observe the consent procedure;
8) Propose changes to HEC standard procedures in a way that is consistent with scientific and technological advancements, as well as changes in human research regulations or criteria on national and international scales;
9) Cooperate with the CMU Ethics Committee in compiling the annual report giving an overview of HEC's performance to RIHES executives; and
10) Engage in other assignments determined by the RIHES Director within HEC's capacity.

1.5 Basic Ethical Principles

Human research must be conducted based on three ethical principles outlined in the Belmont Report, as follows.

1.5.1 Respect for Persons

1) *Respect for human dignity*, rights, faiths, beliefs, feelings as well as traditions and cultures of the human subjects.
2) *Respect for vulnerable persons*, who have impaired decision-making capacity or factors affecting their decision-making. Special measures must be implemented to protect the rights of vulnerable groups, including patients with no prospect of cure, patients with stigmatised illnesses,

individuals with impaired decision-making capacity, elderly in care homes, homeless individuals, foetus, inmates, users or distributors of drugs or other illegal goods, migrants/refugees, children in foster homes, and individuals incapable of communicating in Thai, among others.

3) *Free and informed consent* must be obtained through a sufficient provision of research information covering the contents, methodology, rights, and duties without incomplete disclosure and bias, free of coercion, undue influence, and exculpatory language. The subjects have the freedom to participate in the protocol and to terminate consent at any time without providing reasons.
4) *Respect for privacy and confidentiality*, including permission to approach the person or access personal information and data confidentiality. Unauthorised persons are prevented from accessing the confidential data and the data is destroyed when appropriate.

1.5.2 Beneficence

1) *Risks to subjects are minimised*. Risks to subjects are minimised and subjects will not face unnecessary risks from the research. A minimum sample size that will achieve research objectives and yield statistically analysable data should be used.
2) *Benefits are maximised*. Anticipated benefits, physical or psychological, for subjects are fairly maximised. Further, collective benefits for society and academia must be considered. In the case of adverse events or research harms, the investigators must take responsibility for the treatment or the compensation for damages directly caused by the research procedures.
3) *Risks to subjects are reasonable in relation to anticipated benefits*. There must be a balance between anticipated risks and benefits. The risks must be acceptable to the subjects and approved by HEC.

1.5.3 Justice

1) *Fairness in distribution*. The subject selection must be fair and non-discriminatory of sex, ethnicity, religion and culture without sound reasons. Distribution of anticipated risks and benefits to subjects must

be conducted fairly and reasonably, for instance, not choosing to study a risk group for the benefit of another.

2) *Special protection for vulnerable groups*. Research participants with financial difficulty, children in foster homes, ethnic minorities, inmates, psychiatric patients and individuals with limitations in accessing healthcare must not be recruited on the ground of easy recruitment and management or for the benefit of more privileged groups.

Chapter 2
Guidelines

2.1 Definition of Human subject research

Human subject research is research in which an investigator (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Human subject research covers human subject research and experimentation of pharmaceutical products, medical equipment, the natural history of disease, diagnosis, treatment, health promotion, disease prevention, and research from medical records and human specimens, as well as sociological, psychological, behavioural and economic interviews, designed systematically to test hypothesis and obtain generalisable knowledge.

2.2 Guidelines

1. Investigators must complete training in human research ethics and include evidence of completion when filing for protocol approval. The evidence of completion is valid for three years.
    A. Investigators should attend the Human Subject Protection training, which is a part of the CITI Programme, or any other training programmes organised by any universities or organisations of which the contents cover the Federal Policy for Protection of Human Subjects.
    B. Investigators conducting a clinical trial should attend a hood clinical practice programme either by the CITI Programme or any university or organisation of which the contents cover the ICH Good Clinical Practice (ICH GCP).

** The evidence of completion is signed and certified with the date of signature indicated.

2. Investigators should follow the following principles/guideline:
    A. The Declaration of Helsinki
    B. The Belmont Report
    C. The ICH GCP

3. Investigators must disclose any conflict of interest in the protocol, especially financial ones.
4. Investigators must obtain a Certificate of Approval (CoA) from HEC before their research can begin.
5. After the project has been approved, investigators must follow the approved project. Any amendment to the protocol must be approved by HEC before implementation unless such amendment is done with urgency to protect the welfare of the participants.

   Any action done to protect participants*' safety must be reported within three working days, including a prevention plan for the future. Any amendment to the protocol or consent documents must be submitted for approval.*
6. Investigators of a protocol that has been approved in the HEC meeting must report the progress and if they are unable to finish the protocol and wish to continue with the research, they must renew the CoA 30 days before the expiration date with a copy of the CoA/memorandum indicating the expiration date enclosed.

   6.1 For convened review

   A. In the case of a Progress Report submitted within 30 days before the expiration date as indicated in the CoA, HEC shall consider renewing the CoA from the expiration date or the date of signature by the HEC Chair in the case of amendments.
   B. In the case of a Progress Report submitted before the 30-day-before-expiration period, HEC shall consider renewing the CoA from the date of approval or the date of signature by the HEC Chair in the case of amendments.
   C. In the case of a Progress Report submitted after the expiration date, the Protocol Deviation/Violation Report Form must be enclosed with solutions and prevention methods specified. HEC shall consider renewing the CoA from an appropriate date, as well as allowing the use of data collected during the post-expiration period and conditions (if any) following the meeting's resolutions. Investigators should not accept subjects after the expiration date

and should temporarily halt research activities, except ones that are necessary for the subjects' safety, until they receive the HEC's renewal approval.

6.2 Expedited Review

A. In the case of a Progress Report submitted within 30 days before the expiration date as indicated in the CoA, HEC shall consider renewing the CoA from the expiration date or the date of signature by the HEC Chair in the case of amendments.

B. In the case of Progress Report submission before the 30-day-before-expiration period, HEC shall consider renewing the CoA from the date of approval or the date of signature by the HEC Chair in the case of amendments.

C. In the case of Progress Report submission after the expiration date, the Protocol Deviation/Violation Report Form must be enclosed with solutions and prevention methods specified. HEC shall consider renewing the CoA from an appropriate date, as well as allowing the use of data collected during the post-expiration period and conditions (if any) following the meeting's resolutions. Investigators should not enrol any more participants after the expiration date and should temporarily halt research activities, except ones that are necessary for the subjects' safety, until they receive the HEC's renewal approval.

6.3 For protocols filing for exemption:

HEC has resolved that investigators do not need to submit a Progress Report on the ground that the research poses a low risk and there is no cause for reviewing the report.

7. For protocols approved by expedited review, the CoA is valid for one year and investigators are not required to submit a Progress Report. However, if investigators are unable to complete their research, they must file for renewal and provide reasons for incompletion within a month before the CoA's expiration date, with a copy of the CoA/memorandum indicating the expiration date enclosed.
8. Investigators must report:

A. Any internal SAE taking place within RIHES that causes death or is life-threatening to the subjects. The principal investigator shall report the event to the HEC Chair in writing within 24 hours of being informed. In the case of a non-fatal or life-threatening event, the event shall be reported within seven calendar days after the investigator is informed about the event;

B. Any internal suspected unexpected serious adverse reaction (SUSAR)/unanticipated problem (UAP) that causes death or is life-threatening to the subjects within seven calendar days after the sponsor has confirmed the SUSAR or after the investigator is informed about the event to HEC. In the case of an incomplete preliminary report, a complete report shall be submitted within eight subsequent calendar days and a follow-up report within 15 calendar days;

C. Any local suspected unexpected serious adverse reaction (SUSAR)/unanticipated problem (UAP) that is non-fatal or life-threatening to the subjects within 15 calendar days after the sponsor has confirmed the SUSAR or after the investigator is informed about the event to HEC. A follow-up report must be promptly submitted. In addition, SUSARs in placebo groups do not fall under the criteria of reporting, unless they are caused by contaminants or excipients;

D. Any other non-local adverse event that may increase the risk to the subjects. The principal investigator must report to the HEC Chair promptly within 15 calendar days after being informed;

E. Any other non-local SAE/SUSAR using the CIOMS Report format or any other standard formats sufficiently covering the same information within the period indicated in the project or by the research sponsor, or every six months but no more than a year (periodic or annual safety report);

G. The Safety Report by Data Safety Monitoring Board (DSMB) using Form *HEC F56*

- The sponsor must report any significant change that increases the risk to the subjects and new issues that negatively impact the

participants' or subjects' safety or the research operation to HEC within 15 days of observing the change.

- The sponsor must report DSMB's suggestions promptly within 15 days of receiving them from DSMB.

H. The Safety Information of the Research Product (Investigator's brochure/package insert) using From *HEC F56*

I. Any local or internal adverse event (AE) in an annual report form along with the Progress Report Form in *HEC F38* (along with reviewed SAEs/SUSARs/UAPs).

Investigators can refer to the definition of terms under 'Achieving Guidance in Clinical Trial Safety Information among Stakeholder' by the Forum for Ethical Review Committee in Thailand (FERCIT), June, 2011, and in the Glossary at the end of the Appendix.
(http://www.fercit.org/file/AE_Guidance_publish.pdf)

9. Investigators must report any protocol deviation/violation/non-compliance:
   A. that significantly impacts the participants' welfare or the data integrity within seven calendar days of being informed about the event, as well as specify the corrective action and/or preventive action plan;
   B. that does not significantly impact the participants' welfare or the data integrity within fifteen calendar days of being informed about the event, as well as specify the corrective action and/or preventive action plan.
10. Investigators or sponsors must report premature termination or temporary suspension within 15 calendar days along with a proposed follow-up treatment plan for the subjects.
11. Investigators must submit their Final Report within three months after the results are concluded, with an exception for a multicentre study in which RIHES is one of the research sites, in which case the closure can be reported at RIHES without having to submit the research conclusions.
12. Investigators shall comply with the Researcher Ethics and Practices by the National Research Council of Thailand (NRCT).

2.3 Submission for Review

Investigators may submit their protocols for review in three categories by the degree of risk, as follows.

1. Submission for *exemption review* applies to research with very minimal risk that only causes inconvenience and meets the criteria and lists in **Appendix 1**. After HEC has approved the exemption, investigators are not required to submit a Progress Report. However, any amendment in the project must be approved and a Final Report must be submitted once the process is complete and conclusions have been reached. Exemption review is done by the HEC Secretary within 10 working days. HEC has the authority to consider the case under expedited review or convened review if it is deemed that the risk exceeds inconvenience or that there are issues to be deliberated.
2. Submission for *expedited review* applies to minimal risk research that meets the criteria and lists in **Appendix 2**. The HEC Chair shall appoint no more than two members to assess and present the assessment result to the Chair. After HEC has issued the CoA, investigators are not required to submit a Progress Report. However, if the research cannot be completed within the period indicated in the CoA, a renewal request must be submitted before the CoA's expiration date with the reasons specified. Any amendment must be approved before implementation, and a Final Report must be submitted once the process is complete and the conclusions have been reached. Expedited review shall take no more than two weeks. In addition, expedited review applies to minor changes, Progress Reports approved at the convened meeting and other reports that meet the criteria (**See Appendix 3**). HEC has the authority to take the case to convened review if it is deemed that the risk is greater than minimal or that there are issues to be deliberated.
3. *Convened review* applies to greater than minimal risk research that requires full board review. Investigators must submit a Progress Report as a part of the renewal request before the COA's expiration date. Any modifications must be approved before implemented and a Final Report must be submitted once the project is complete.

    The HEC convened meeting takes place once a month. Protocols of which documents are submitted within the specified submission window shall be

reviewed at each meeting. ORE shall administer the annual meeting plan. The submission window for each meeting may change from the annual meeting plan. The Office shall announce any changes on the website or via e-mail notifications.

2.4 Preparing Documents for Submission

Investigators must submit the Form for Ethical Approval to the RIHES Director and enclose the Director's Note with a list of documents by the category of review to the HEC Chair. Relevant forms are available at https://www.rihes.cmu.ac.th/ore/

2.4.1 Initial Protocols

Three hard copies and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Full Research Protocol in Thai or English	
[ ]	Biographies of the principal investigator and co-investigators that are current, signed and certified with a date	
[ ]	Initial Review Submission Form	**HEC F29**
[ ]	Initial Review Application Form	**HEC F30**
[ ]	Informed consent documents, consisting of • Patient or Subject Information Sheet • Consent Form	
[ ]	Certificate(s) of translation for informed consent documents (if any)*	
[ ]	Broad Consent (if applicable)	
[ ]	Questionnaire/Interview form (if applicable)	
[ ]	Pamphlets, and posters recruiting participants (if applicable)	
[ ]	Investigator's brochure (if applicable)	
[ ]	Case Report Form (if applicable)	
[ ]	Permission letter from the affiliation of the co-investigator from another RIHES department/agency, or another external agency (if applicable)	
[ ]	Certificate of Indemnity or Insurance for compensation in the case of patient's or subject's sickness due to research participation (in	

	the case of the sponsor being a private funding body and the research being a product research)	
[ ]	Material Transfer Agreement (if applicable)	

* In the case of a certificate of translation, HEC shall only suggest corrections on parts which are deemed incorrect or likely to cause misunderstanding to participants.

2.4.2 Protocols Resubmitted After Revision Following HEC Recommendations and Re-reviewed at Convened Meeting

Three hard copies and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Summary of Changes for Additional Changes/Revisions Following HEC Decisions	**HEC F36**
[ ]	Resubmitted documents in two versions: track change and clean file in PDF format	
[ ]	Other relevant documents	

2.4.3 Protocols Resubmitted After Revision Following HEC Recommendations and Granted Approval

Two hard copies and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Summary of Changes for Additional Changes/Revisions Following HEC Decisions	**HEC F36**
[ ]	Other relevant documents	

2.2.4 Protocols With Amendments

Two hard copies and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Protocol Amendment Review Form	**HEC F37**
[ ]	Summary of Changes for Additional Changes/Revisions Following HEC Decisions	**HEC F36**
[ ]	Summary of the revised protocol	

[ ]	Other relevant documents	

2.4.5 Progress Report

Two hard copies and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Current research protocol	
[ ]	Progress Report Form with reports on internal SAEs/SUSARs/UAPs (if any)	**HEC F38**
[ ]	Current version of informed consent documents	
[ ]	HEC notification of approval to proceed or renew (in the past year)	
[ ]	Other documents that require HEC's approval for continued use	

2.4.6 Final Report

One hard copy and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Final Report Form	**HEC F39**
[ ]	Other relevant documents (if any)	

2.4.7 Report of Premature Termination or Temporary Suspension

One hard copy and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Report Form for Premature Termination or Suspension	**HEC F43**
[ ]	Other relevant documents e.g. reports by DMSB or sponsors (if any)	

2.4.8 Safety Report

A. Reporting local SAEs/SUSARs/UAPs

Two hard copies and one electronic copy of each are required for submission.

	Document List	Form
[ ]	Internal SAE/SUSAR/UAP Report Form	**HEC F44**
[ ]	External SAE/SUSAR/UAP Report Form	
[ ]	DSMB Report	**HEC F56**

[ ]	Safety Information of Research Product (Investigator's brochure/Package Insert)	**HEC F56**
[ ]	Other documents:	

For reporting a single case, use Form *HEC F44*, the CIOMS Form or other standard forms sufficiently covering the following list of information.

1) Protocol title
2) Date of event
3) Subject information
4) Disease(s)/illness(es) prior to enrolment to the study
5) Other medications or medical devices received from the study
6) Event
7) Results of event (severity)
8) Relation of event to medications or medical devices used in the study

For reporting multiple cases, follow the same list as the single-case report.

B. Reporting internal SAEs occurring <u>at</u> RIHES

Two hard copies and one electronic copy of each are required for submission.

The principal investigator shall submit a written report to the HEC Chair within 24 hours (in the case of deaths or life-threatening events) of being informed, or seven calendar days (in the case of non-fatal or non-life-threatening events) of being informed. Use Form *HEC F44*, the CIOMS Form or other standard forms sufficiently covering the same information.

C. Reporting internal SUSARs/UAPs occurring at RIHES

Two hard copies and one electronic copy of each are required for submission.

Reporting multiple cases shall be done in the same manner as a single-case report. The primary investigator shall submit a written report to the HEC Chair within seven calendar days (in the case of SUSARs/UAPs causing deaths or life-threatening events) after the sponsor has confirmed or after the investigator has been informed about the event. If the preliminary report is incomplete, the sponsor shall report relevant information obtained from the follow-up investigation to the HEC Chair and complete the report within eight subsequent calendar days. New, important information shall be reported in a follow-up report by the sponsor to the HEC Chair within 15 calendar days.

Any non-fatal and non-life-threatening event shall be reported within 15 calendar days after the sponsor's confirmation, using Form *HEC F44*, the CIOMS Form or other standard forms sufficiently covering the same information.

D. Reporting external SAEs occurring outside RIHES

Two hard copies and one electronic copy of each are required for submission.

The primary investigator shall promptly report external SAEs to the HEC Chair within 15 calendar days (in the case that the SAE may increase the risk to the subjects) of being informed, using the CIOMS Form or other standard forms sufficiently covering the same information.

E. **Reporting external SUSARs/UAPs occurring outside RIHES**

Two hard copies and one electronic copy of each are required for submission.

The primary investigator shall report to the HEC Chair within the period specified in the protocol or by the sponsor, or every six months but no more than one year (periodic or annual safety report) in the form of a summary report written in English following the CIOMS format or other standard formats sufficiently covering the same information, using the CIOMS Report Form or other forms sufficiently covering the same information.

F. DSMB Report using Form *HEC F56*

- The sponsor shall report any significant change that results in the increase of risk to subjects and new issues that negatively impact the safety of the subjects or the research procedure to HEC within 15 calendar days of observing the change.
- The sponsor shall promptly report the suggestions by DSMB within 15 calendar days of receiving them.

G. Safety information of Research Product（Investigator's brochure/Package Insert) using Form *HEC F56*

H. Reporting internal AEs

The primary investigator shall summarise internal AEs and report to the HEC Chair in the annual Progress Report *HEC F38* along with a summary report of SAEs/SUSARs/UAPs that have been reviewed.

2.4.8 Submitting other documents

Other documents not mentioned in the above lists such as protocol team's reports, newsletters and others

One hard copy and one electronic copy of each are required for submission.

	Document List	**Form**
[ ]	Relevant documents translated into Thai	-
[ ]	Relevant documents in the English version	-

2.5 Labelling Version/Date of Submitted Documents

Submitted documents such as protocols and ICFs must have the version number and date indicated in the document's footer for reference purposes in the approval document. The submitted version should be labelled 'Version 1.0' and for each amendment, the number shall increase accordingly.

2.6 Submission Location

Investigators submit the hard copies of the documents at the Office of Research Ethics (ORE), on the third floor, Room 234, and the documents will be checked against the requirements. The checking officer shall notify the investigator If any documents are incomplete. Once all documents are complete, they will receive an acceptance stamp with a reference number, the date of acceptance, and the document recipient's name. The electronic copy shall be submitted to rihes.hec@gmail.com.

2.7 Notification of Result

ORE officers will notify the unofficial result via e-mail of the investigator or the protocol's coordinator within five working days after the day of the HEC meeting or after the day that the HEC Secretary has concluded the review result by the Reviewing Committee (in the case of expedited review). The official result shall be notified according to the RIHES administrative protocol.

2.8 Certificate of Approval (CoA) Renewal

CoA is issued on a yearly basis. The HEC Secretary shall send a letter notifying investigators 45 days before the expiration date. Investigators must submit a Progress Report and request for renewal (if desired).

(A) Protocols approved by convened review – If investigators submit the protocol within 30 days before the expiration date, the renewal will start from the date of expiration. However, if the 30-day period is exceeded, the renewal will start from the date on which the renewal is approved or the Chair gives approval (In the case of recommendation for revision).

(B) Protocols approved by expedited review – Investigators should submit the renewal request within 30 days before the expiration date with reasons for incompletion specified. The Chair will approve the renewal from the expiration date without reviewing a Progress Report.

(C) For submission after the expiration date:

i. This falls under noncompliance. Investigators must suspend subject enrolment once the CoA has expired and report the noncompliance to HEC as soon as informed.

ii. HEC shall not review the renewal request if it has not received a noncompliance report.

iii. HEC may not permit the use of data collected from subjects during the expired period. Cases will be reviewed on a case-by-case basis.

2.9 Major Changes and Resubmission

In the case of major changes and resubmission, investigators should make major changes and resubmit within 60 days. If longer, the scientific value may be affected, as other institutions may already have reported a study addressing the same issue.

2.10 Final Report (Completed Within Schedule)

Completion of research activity following the plan is considered a change in the protocol and thus must be reported to HEC. The criteria for research completion within the schedule are as follows.

iv. The number of enrolled subjects is according to the plan and the research activities approved by HEC are completed.

v. The collection, use and analysis of identifiable data are complete and data or tissue samples are no longer collected from the subjects.

vi. The Final Report or the manuscript is finished (except for a multi-centre research, in which the principal investigator takes the responsibility).

2.11 Storage of Relevant Documents

In the case of investigator-initiated research, research documents shall be stored for at least five years or as indicated by RIHES or the sponsor regulations, and then destroyed using accepted methods.

i. Paper documents shall be destroyed using a shredder.
ii. Computer files shall be deleted permanently from the hard disk or zipped with a password and stored in a password-protected personal computer.

Pharmaceutical-sponsored drug trials shall follow the regulations of the sponsor.

2.12 Guidelines for Review Submission for Research in Collaboration with Personnel from the Faculty of Medicine, Chiang Mai University

RIHES has an MoU regarding human research review with the Faculty of Medicine and Chiang Mai University specifying that protocols approved by HEC shall not be re-reviewed by the Faculty of Medicine. This criterion applies exclusively to RIHES researchers intending to conduct research projects with personnel from the Faculty of Medicine and/or personnel from the Faculty of Medicine as co-investigator.

Investigators of protocols that meet this criterion shall proceed as follows.

1. Submit the Initial Review Submission Form and relevant documents to HEC and once the protocol is approved, investigators must submit the initial protocol/amendment/Progress Report/other reports and relevant documents, as well as the HEC review result to the Faculty of Medicine's Research Ethics Committee, who will not re-review the protocol but will grant approval promptly as per the agreement by both parties. However, the primary investigator should discuss this with the sponsor beforehand. If the sponsor requests that the two committees review the protocol independently, the primary investigator must comply and request in the submission form that the Faculty of Medicine re-review the protocol independently.
2. Any amendment/Progress Reports/other reports shall be submitted in the same manner as in no 1.
3. Other reports such as the SAE Report or the Protocol Deviation Report are submitted only to RIHES.

However, this agreement does not apply to phase-1 clinical trials and is fully effective for new protocols from the date of signature of the MoU.

Appendix

Appendix 1

Types of Activities and Research Eligible for Exemption Review

1. Non-research Protocols

1.1 Teaching activities, educational quality assurance, hospital quality assurance, quality improvement and service evaluation, all of which must adhere to the guidelines set by quality assurance committees or other board committees

1.2 Case reports of no more than three cases in which appropriate confidentiality protection has been demonstrated by the requester (Remark: Investigators should be aware that several academic journals may require that there be informed consent forms to use patient data or images.)

2. Protocols Under the Following Categories

2.1 Research not involving humans as subjects or collection of identifiable personal information or biospecimens

2.2 Research conducted at RIHES or other educational institutions on academic service (e.g. educational strategy research, effectiveness research or comparison of teaching methods, curricula or classroom management which are conducted following standard protocols without added measures)

2.3 Research by survey and interview that must not:

(1) Involve sensitive topics/questions such as sexual behaviours, illegal behaviours and behaviours causing damage to the reputation of any person/community;

(2) Ask about attitudes that, if disclosed, may cause negative consequences on employment such as satisfaction survey of government officers on received welfare;

(3) Yield results that cause damage to the reputation of the informant organisation;

(4) Record data in a manner that leads to identification either directly or through codes.

2.4 Research conducted by observation of public behaviours in public spaces that do not:

(1) Involve intervention or arrangement by investigators;

(2) violate privacy through observed behaviours or locations;

(3) Record data in a manner that leads to identification either directly or through codes.

2.5 Research involving the collection of identifiable private information or identifiable biospecimens that fall into one of the following categories: (A) are disclosed to the public as required by the law or are not expected to be confidential; (B) are not recorded in a manner that leads to identification either directly or through codes, and investigators do not contact or track owners of the personal information/biospecimens.

2.6 Research that uses anonymous secondary data such as data from organisational annual reports or diagnosis records.

2.7 Laboratory research that uses samples from commercial sources such as cell lines purchased from ATCC or given by other laboratories, and adheres to material transfer agreements (if any).

2.8 Retrospective research studying leftover specimens stored in the inventory of the organisation established and approved by HEC, and the use of samples follows the regulations of the biological sample inventory.

2.9 Consumer taste, quality, and satisfaction evaluations in which (A) the food is of health benefits without additives or contaminants; or (B) in the presence of additives or contaminants, evidence showing that the level does not exceed the limit of the FDA or other related agencies.

Types of Research Ineligible for Exemption

Protocols ineligible for exemption include:

(1) Research that involves incomplete disclosure or deception;

(2) Research on the following groups:

A. Individuals under strict protection to which permission to access is required such as inmates, minors in juvenile detention centres, elderly or children in care homes, refugees/migrants in camps and patients being treated at mental healthcare facilities;

B. Individuals with severe extremely vulnerable mental conditions such as teenage mothers, individuals with suicide or self-harm history, individuals

with major depressive disorder and sufferers from post-traumatic stress disorder.

(3) Research of which the results have the tendency to lead to speculation about the identity of a group of individuals or a community, and may cause damage to reputation or lead to lawsuit;

(4) Research involving incomplete disclosure or deception.

Appendix 2

Types of Activities and Research Eligible for Expedited review

1. Protocol amendments that are minor changes that present no more than minimal risk to participants or do not significantly change the risk/benefit balance assessment.
2. Research that involves the use of interview/questionnaire and data recording in an identifiable manner either directly or through codes, but does not involve sensitive personal information (e.g. sexual orientation) and cause damage to the status or benefits of the person if disclosed, and does not violate the sensitivity of related populations.
3. Research that involves a collection of a small quantity of blood samples that is not performed too frequently, for example, from fingertips, heels or eartips.
    A. In the case of healthy adults weighing at least 45 kg, the amounts drawn may not exceed 550 ml in eight weeks and collection may not be performed more frequently than two times per week.
    B. In the case of children or patients, the weight, illness, collection method and frequency shall be taken into account. The amounts drawn may not exceed 3 ml per kg in eight weeks and collection may not be performed more frequently than two times per week.
4. Research that involves a non-invasive collection of biospecimens (e.g. fluid and excrement collection or nail clippings in a non-disfiguring manner).
5. Data collection for research purposes using non-invasive methods (not involving the use of anaesthesia or sedation) commonly practised in medicine and authorised use of medical devices e.g. EEG or ECG, acoustic testing, Doppler test, non-invasive blood pressure measurement, general examination, and general physical fitness test using exercise. However, uses of X-ray or microwave radiation or MRI are not eligible for expedited review.
6. Research that involves data, documents or specimens that have been collected or will be collected from patient treatment or diagnosis (names, name records or identifiable codes may be known).
7. Research that involves personal traits or groups of individuals, or uses surveys, interviews, history taking or focus groups.

8. Progress report/extension request for protocols approved by HEC in which: (A) no research activity on participants has begun; (B) participants are no longer accepted or all participants have received the prescribed amount of medications/procedures and the only remaining activity is participant follow-up; or (C) no additional participants are enrolled and no added risk is present; or (D) the remaining activity to be performed is data or biological sample analysis.
9. Protocols that have been instructed by HEC to make changes and then are submitted for expedited review.
10. Reports of protocol deviations that are necessary to eliminate immediate hazards to participants.
11. DMSB reports indicating no changes in the safety data that affect participants.
12. Revised safety information of research products (investigator's brochures/package inserts).
13. IND Safety Reports that have undergone review but are resubmitted by investigators from another institution due to the protocol being a multi-centre research.
14. Research in which mild behavioural intervention in adults is involved and responses are collected in speech or text, or video and audio recording. Mild behavioural intervention refers to short-period interventions that do not cause harm, pain, and physical invasion and are unlikely to cause remnant adverse effects on participants, and investigators do not believe that participants will perceive such interventions as offensive, aggressive or humiliating. Examples of behavioural interventions that do not cause harm include having participants play an online game, solve a puzzle under a noisy condition or decide how to distribute the money received (during the game) to self and others.
15. Establishment of biological sample/research data inventory by using broad consent for future research.

Expedited review does not apply to an initial protocol which:

(A) Puts participants at risk of criminal or civil liabilities, or negative consequences in terms of financial, employment, insurance, reputation, or social exclusion e.g. research on behaviours that violate the laws, organisational regulations or social norms if participants' identities of and/or responses are disclosed;

(B) Involves incomplete disclosure or deception;

(C) Is experimental research;

(D) Involves the following groups;

A. Individuals under strict protection to which permission to access is required such as inmates, minors in juvenile detention centres, elderly or children in care homes, refugees/migrants in camps and patients being treated at mental healthcare facilities;

B. Individuals with severe extremely vulnerable mental conditions such as teenage mothers, individuals with suicide or self-harm history, individuals with major depressive disorder and sufferers from post-traumatic stress disorder.

Appendix 3

Types of Protocol Change

1. Protocol Amendment

Protocol amendment refers to changes and descriptions of details officially added to the protocol in writing.

2. Minor Change

Minor change refers to additional changes that present no more than minimal risk to participants or do not significantly change the risk/benefit balance assessment.

3. Major Change

Major change refers to additional changes that present more than minimal risk to participants or significantly change the risk/benefit balance assessment.

4. Summary of Changes

Summary of Changes refers to the document indicating amendments, deleted or added statements and reasons for deletion or addition.

Examples of minor and major changes

Minor Change	Major Change
— Correcting typographical errors or writing style that still retains the original meaning — Changing investigator(s) or contact address — Changing protocol management — Minor changes in the recruitment method or the recruitment document following the approved method — Minor changes in the questionnaire or survey — Slight changes in compensation for the participants	— Adding genetic tests, new genetic testing methods or storage of tissue samples in an inventory for generic testing — Adding an open trial after effectiveness trials — Urgent changes that have already been implemented to ensure the participants' safety and are subsequently reported in the protocol — Changing the research objective(s) — Changing the dosage or the drug administration method

— Increasing the amount of blood drawn because the previous amount was insufficient for analysis — Submitting the translated version of an approved document — Updating the investigator's brochure — Changing the recording format — Changing the method of transferring/accepting samples — Increasing sites (unrelated to new trials of new drugs or medical devices) — Extending the time period from the amount indicated in the submission	— Reducing the follow-up frequency — Change of recruitment method that affects the confidentiality that may cause exposure, harassment or fear of offending — Changing the experimental method — Changing the population — Adding or removing a treatment — Changing the inclusion or exclusion criteria — Increasing or decreasing the sample size at a great quantity, for instance, In the case of the original size being less than 20, the increase or decrease is over 5; or In the case of the original size being greater than 20, the increase or decrease is greater than 20 per cent. — Changing the characteristics of the sample group, which affects the original objective, or adding vulnerable participants — Increasing sites (unrelated to new trials of new drugs or medical devices) — Changing the primary investigator — Changing the criteria for research closure

Appendix 4
Suggestions for Creating Informed Consent Documents

Informed consent documents are composed of two parts: the participant information sheet and the consent form. Once signed by participants, investigators must give one copy of the documents to participants.

Signing the informed consent form is the standard protocol but, in some cases, investigators may request a waiver of informed consent, modify the informed consent information or request a waiver of signed consent. However, they must state their intent to HEC with reasons explaining the necessity specified.

Documents for participants should cover the following contents.

(1) Statements explaining the nature of the research, research objectives, duration of participation, research methodology, and experimental methods
(2) Risks and discomfort that may occur to participants
(3) Benefits that participants or others may receive from the research
(4) Other alternatives or treatment options (if any) that may benefit participants
(5) Confidentiality process for identifiable data
(6) For research that exceeds minimal risk, whether treatment and injury compensations are provided must be specified with a clear description of the components and information sources.
(7) Contact person for inquiry about the research and participant rights, and injuries that occurred during the research
(8) Statements indicating that participation is voluntary, In the case of refusal, participants will not be penalised or otherwise lose entitled benefits as a result; and that participants may terminate participation at any time without being penalised or losing entitled benefits as a result.
(9) One of the following statements on research involving a collection of identifiable personal information or biospecimens
    (A) Statements indicating that identifiable elements may be removed from identifiable personal information/biospecimens, and identifiable personal information/biospecimens may be used in the future or distributed to other researchers without asking for consent from the participants or their legal representatives again

(B) Statements indicating that identifiable private information or identifiable biospecimens stored as a part of the research with identifiable elements removed will not be used or distributed for future research

Other required contents that will be added as appropriate:

(1) Statements indicating that medications or procedures may present unforeseeable risk to participants (or embryos or foetus)
(2) Circumstances in which investigators may remove participants from the research without asking for consent from the participants or their legal representatives
(3) Expenses incurred due to research participation that will be covered by participants
(4) Consequences of withdrawing from the research, and process of participation termination
(5) Statements indicating that discoveries made during research that may affect participants' voluntariness to continue participation will be notified
(6) Estimated number of participants
(7) Statements indicating that biospecimens (even with identifiable elements removed) may be used for commercial purposes and whether o not participants will receive their share of income
(8) Statements indicating whether relevant results will be revealed to participants and under what conditions
(9) For research involving biological sample collection, statements indicating whether genome sequencing will be included

Broad consent shall include:

(1) Contents under Items (2), (3), (5), and (8); and (7) and (9) which are added as appropriate;
(2) Statements indicating the type of conducted research on biospecimens and identifiable data, in which explanation must be sufficiently provided to allow reasonable individuals what to anticipate from such type of research;

(3) Statements indicating biospecimens or private information that may be used in the research and the institution type/researcher that will conduct research using the samples/data;
(4) Statements indicating the period of storage of biospecimens or personal information (which may be indefinite) and the period of use of biospecimens or personal information for research (which may be indefinite);
(5) If the research type is not specified in detail, statements indicating that participants or their legal representatives will not be notified about the research's details such as research objectives, or that participants or their legal representatives may choose not to consent to that specific type of research;
(6) Statements indicating that any personal result will not be revealed if it is unrelated to health;
(7) Statements indicating the contact person In the case of inquiry regarding participant rights, storage and use of identifiable private information or biospecimens, or the contact person In the case of harm occurring because of research participation.

Informed Consent Documents

In the case of informed consent documents presented in great length such as in clinical trials, investigators should provide a summary of one to three pages to inform participants based on the Common Rule (2017) and the SACHRP Recommendations, as follows.

> Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.
> For reference, "the elements of consent listed in the preamble" are:
> (1) the fact that consent is being sought for research and that participation is voluntary;
> (2) the purposes of the research, the expected duration of the prospective subject's participation, and the procedures to be followed in the research;

(3) the reasonably foreseeable risks or discomforts to the prospective subject;
(4) the benefits to the prospective subject or to others that may reasonably be expected from the research; and
(5) appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the prospective subject.

SACHRP recognizes that the elements of consent listed in the preamble may or may not be sufficient to satisfy the requirement for providing key information depending on the study.
Examples of additional elements of consent or other information that might be key information in certain studies include:

- Essential study design elements such as randomization, the use of placebo, crossover design, or washout requirements from current effective treatments
- How the treatment in the trial is similar to or different from the clinical care the subject would receive if not in the trial
- Significant costs that could be incurred as a result of participation
- Compensation for injury
- How much time and/or how many research visits are required for participation
- Payments to subjects
- Impact on the subject's future clinical care. For example, whether use of an experimental intervention is likely to make a standard clinical intervention ineffective or unavailable after the study
- Potential impact on non-participants. Examples include caregivers, family members, children, partners and the public.
- Post-trial access to the experimental intervention

For further information:

Attachment C -New "Key Information" Informed Consent Requirements. SACHRP Commentary on the New “Key Information” Informed Consent Requirements. October 17, 2018

[https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html]

Separating Informed Consent Documents

Investigators should have a separate set of the main informed consent documents as shown in the main research objectives, and in the case of leftover specimen storage or additional collection for future use, there should be another set for broad consent. This is because: (A) combining the two sets may become coercive, and (B) contents necessary for the broad consent may differ from the core contents in the main informed consent documents and changes will pose difficulty.

Only In the case of non-clinical-trials may the sample collection be included in the main version.

Guidelines for Creating Information Sheet and Informed Consent Form

- http://www.fercit.org/template.htm
- https://w1.med.cmu.ac.th/research/ethics/ICF.html
- Koonrungsesomboon, N, Tharavanij, T, Shayakul, C, editors. Guidance and template of informed consent form for clinical trials in Thailand [*nǣothāng læ tonbæp ʻēkkasān khǭmūn læ khǭ̄khwām yinyǭm samrap kānwichǎi thāng khlinik nai prathēt Thai*]. Forum for Ethical Review Committee in Thailand; 2020.

Signing the Informed Consent Form

1. Participants over 18 years old are allowed to sign the Informed Consent Form and indicate the date of signature on their own.
2. In the case that the person in Item 1 is an illiterate person, at least one witness who does not have a conflict of interest with the protocol shall sign the Form with the date of signature to testify that the participant has

been fully informed and has given verbal consent in front of the witness. The illiterate participant shall draw a mark or stamp the fingerprint on the Form.

3. In the case of participants of age over 7 but not over 18, assent and parental consent are required.

3.1 In the case of participants of age 13 to less than 18, the same Information Sheet may be used, unless they have difficulty understanding or the nature of the protocol is complex.

3.2 In the case of participants of age 7 to less than 13, the Information Sheet for children must be separate from the one for parents.

3.3 In the case of participants of age less than 7, investigators may obtain assent verbally from the participants in the presence of their parents who will sign the Informed Consent Form.

Asking parents to sign the Consent Form shall follow the following procedure.

1. If the research presents no more than minimal risk or if it presents a minimal risk but may yield direct benefits to the child participants' health, either the father or the mother shall sign the Consent Form.
2. If the research presents greater than minimal risk and does not yield direct benefits to the child participants' health, both the father and the mother shall sign the Consent Form.

After participants have signed the Consent Form, they shall be given a copy of the documents and a copy of the signed Consent Form.

Investigators may request a waiver of documentation of consent if:

1. The written signature on the Consent Form is the only identifiable information the participants and can present potential harm to the participants if the information is leaked or the participation is disclosed. This condition does not apply to drug/device trials.
2. The research presents no more than minimal risk to participants, and does not involve procedures that typically require a signature even if they are unrelated to the research.

Upon requesting a waiver of documentation of consent, investigators should have another method proving that participants have given their consent, for example, voice or video recording in the case of verbal consent.

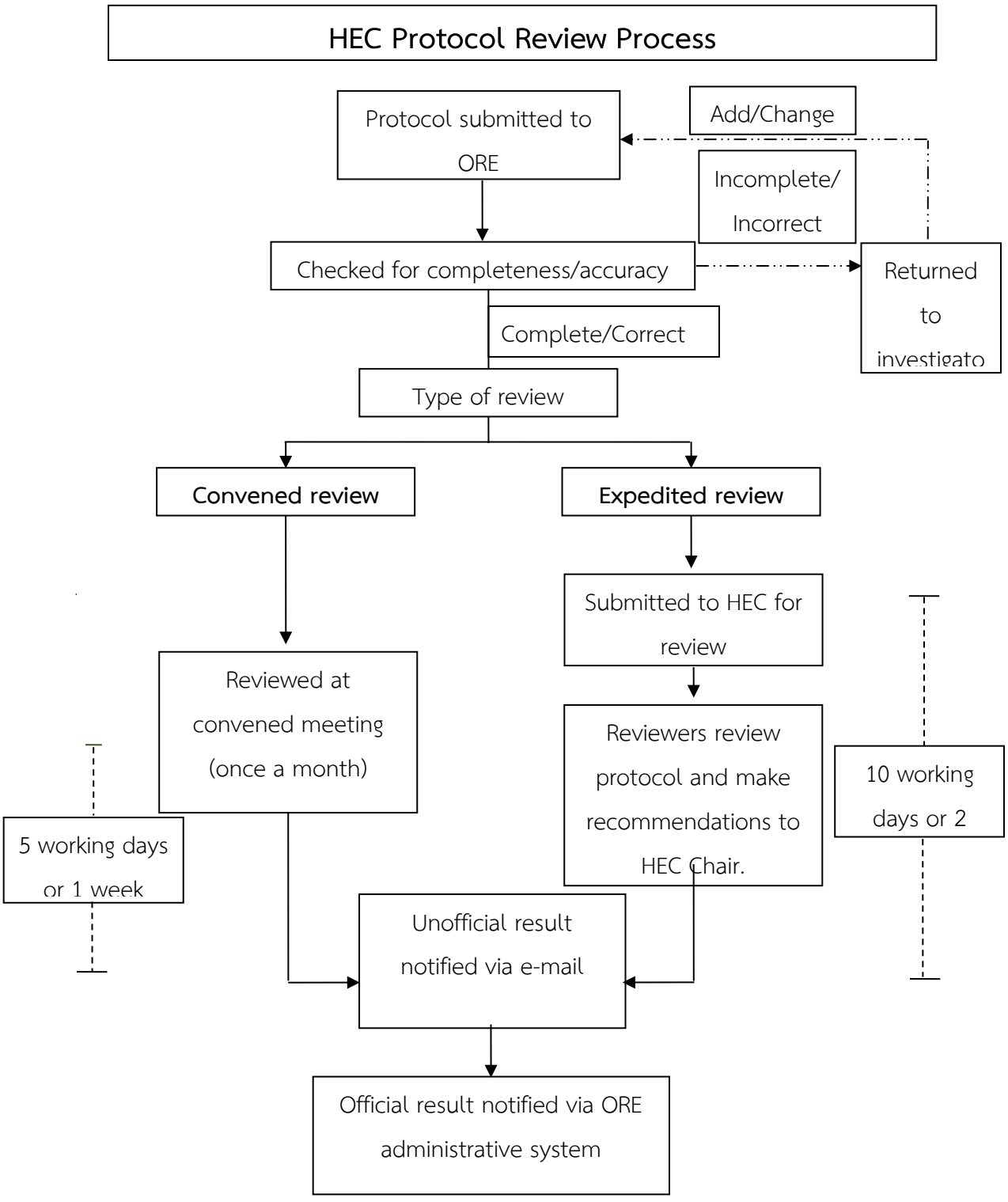
Investigators may request a waiver of informed consent procedure, or give partial or modified information to participants in the case that:

1. The research presents no more than minimal risk to participants and waiving the informed consent procedure, or giving partial or modified information does not affect the rights and welfare of participants. The research cannot be conducted without waiving the informed consent procedure, or giving partial or modified information, and participants will later receive information about the research at the appropriate time;
2. The research is survey research using surveys, telephone or electronic means, in which investigators have informed participants that they have the right to not respond or to decline participation for decision-making purposes. The research does not involve sensitive topics. Participants are not vulnerable persons. The survey return does not involve a direct meeting with participants.

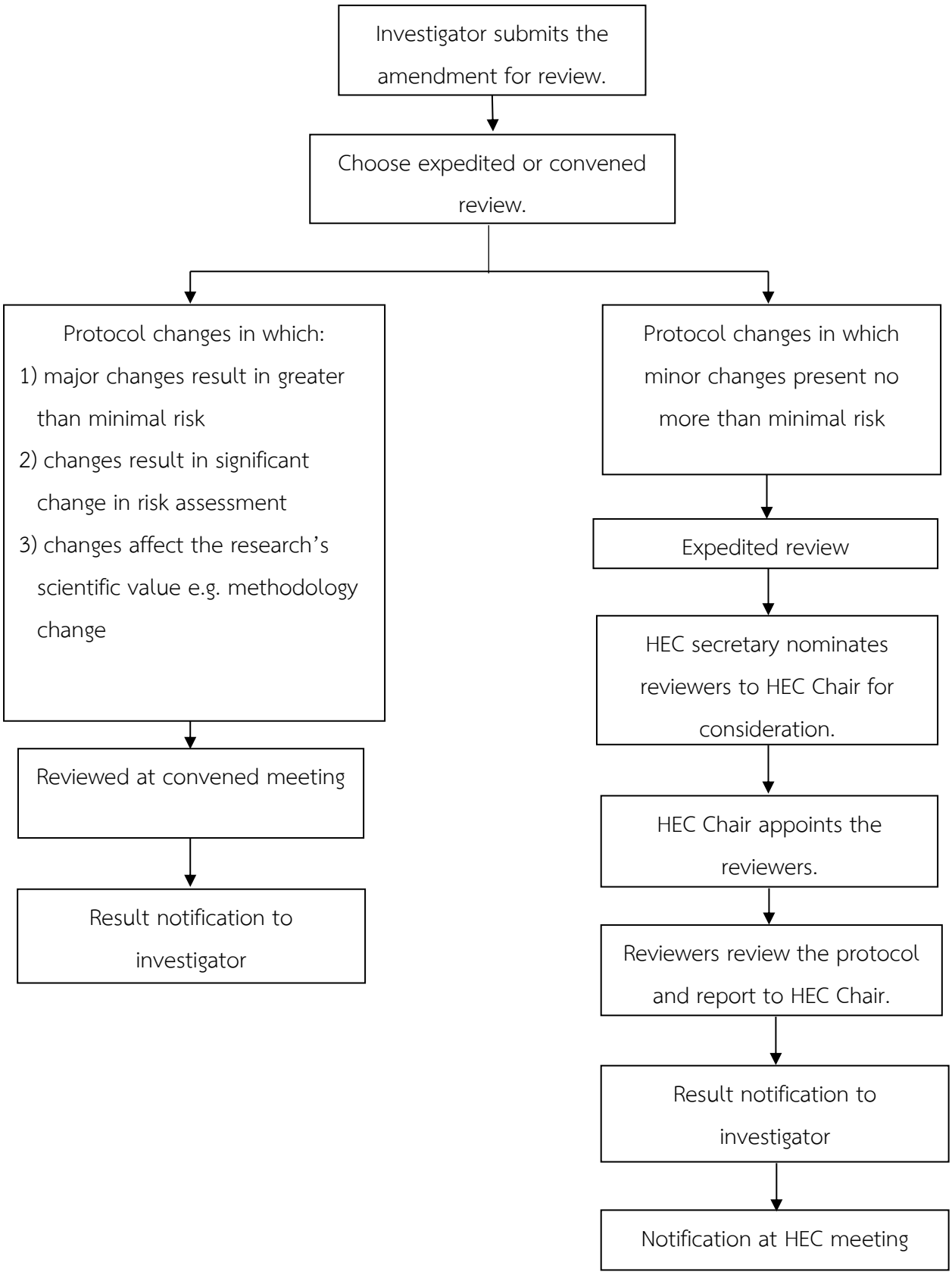
Appendix 5

Flow Chart for Protocol Review

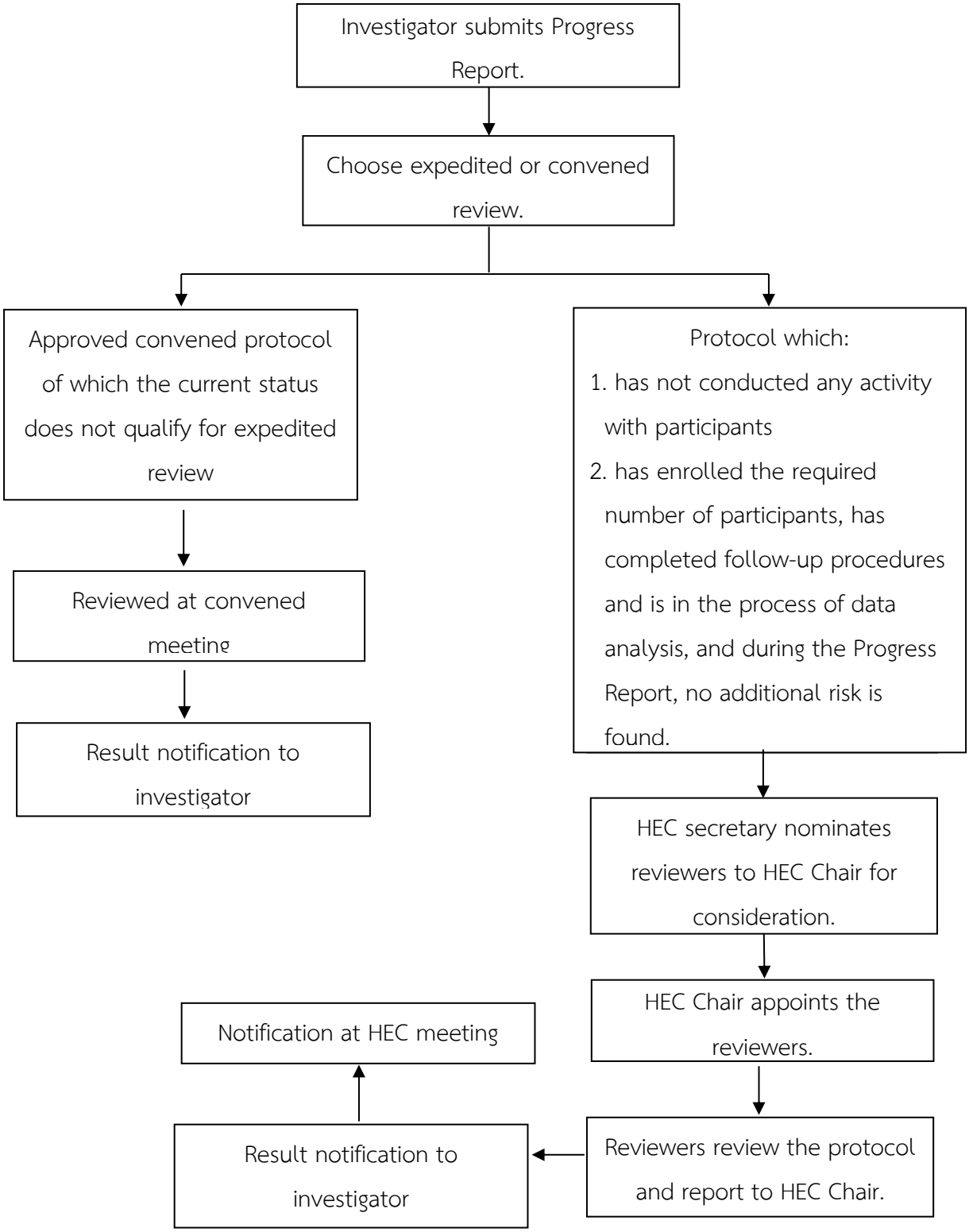
(1) Flow Chart demonstrating HEC Protocol Review Process



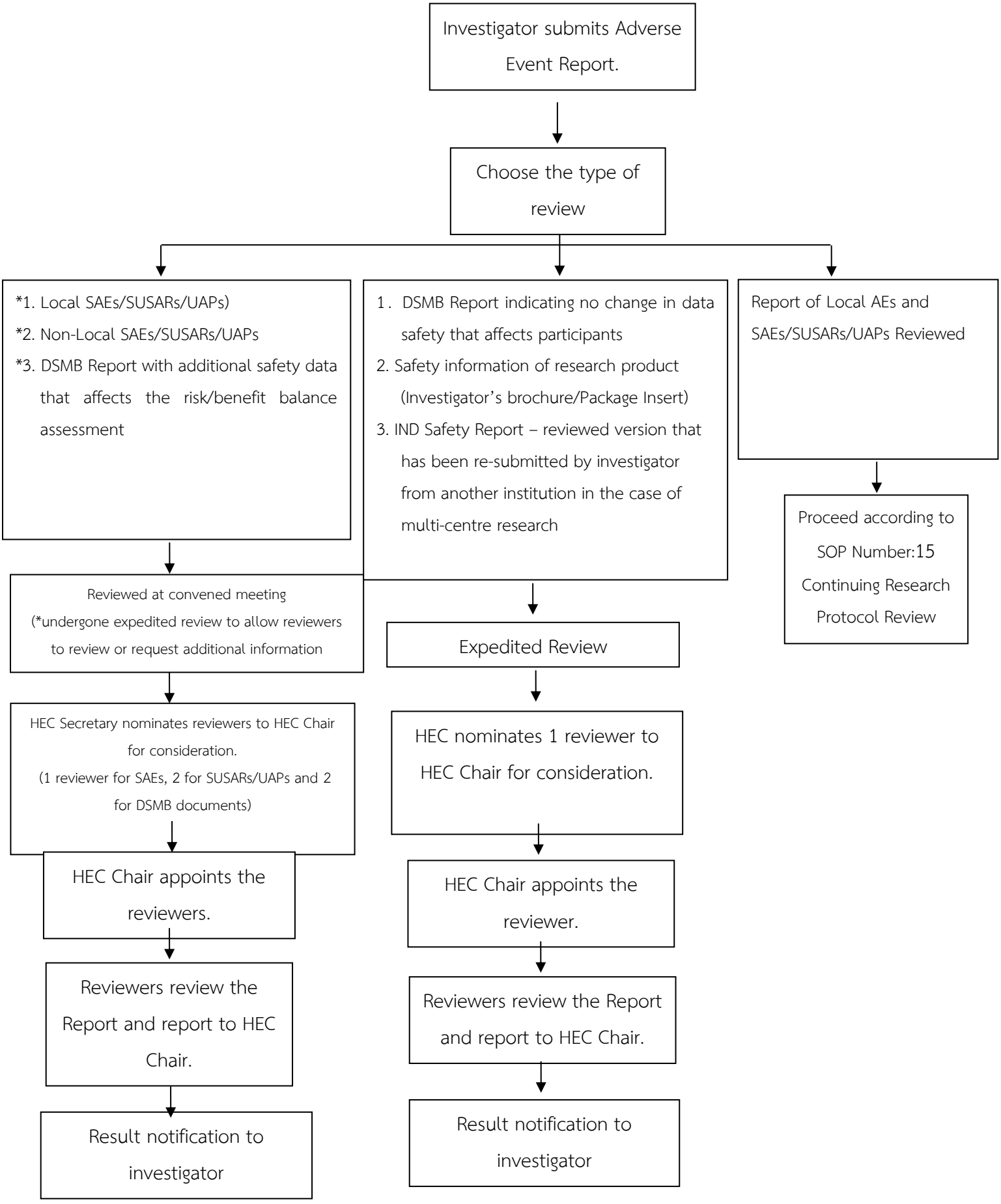
(2) Flow Chart for Amendment Review



(3) Flow Chart for Continuing Research Protocol Review



(4) Flow Chart for Adverse Event Report Review



* Reporting period

1. For any local SAE taking place within RIHES that causes death or is life-threatening to the subjects, the principal investigator shall report the event to the HEC Chair in writing within 24 hours of being informed. In the case of a non-fatal or life-threatening event, the event shall be reported within seven calendar days after they are informed about the event.
2. Any SUSAR/UAP that causes death or is life-threatening to the participant(s) shall report the event within seven calendar days after the sponsor has confirmed the SUSAR or after they are informed about the event to HEC. In the case of an incomplete preliminary report, a complete report shall be submitted within eight subsequent calendar days and a follow-up report within 15 calendar days.
3. Any SUSAR/UAP that is non-fatal or life-threatening to the subjects shall be reported within 15 calendar days after the sponsor has confirmed the SUSAR or after investigators are informed about the event to HEC. A follow-up report must be promptly submitted. In addition, SUSARs in placebo groups do not fall under the criteria of reporting, unless they are caused by contaminants or excipients.
4. For any other non-local adverse event that may increase risk to the subjects, the principal investigator must report to the HEC Chair promptly within 15 calendar days of being informed.
5. Any local adverse event (AE) shall be reported in an annual report form enclosed with the Progress Report Form in HEC F38 (along with the reviewed summary of SAEs/SUSARs/UAPs).
6. Any other non-local SAE/SUSAR shall be reported using the CIOMS Report format or any other standard formats sufficiently covering the same information within the period indicated in the protocol or by the research sponsor, or every six months but no more than one year (periodic or annual safety report).
7. The Safety Report by Data Safety Monitoring Board (DSMB) shall be reported using Form HEC F56.
    - The sponsor must report any significant change that increases risk to the subjects, and new issue that negatively impacts the participants' or subjects' safety and the research operation to HEC within 15 days after observing the change.
    - The sponsor must report DSMB's suggestions promptly within 15 days of receiving them from DSMB.

8. The safety information of the research product (Investigator's brochure/package insert) shall be reported using From HEC F56.

Appendix 6

Examples of Unanticipated Problem Involving Risk to Subjects or Others (UPIRTSO)

[Reference: 45CFR46.103.b.5, 21CFR56.108.b.1 และ 21CFR812.3.s]

Unanticipated problem involving risk to subjects or others (UPIRTSO) may include any unanticipated events resulting from research implementation, studied population, and approved procedures or regulations. These problems are related to the risk to subjects or others (e.g. research staff, family members or others who are not directly involved in the research), and intervention, research procedures and/or implementation. The risk (including physical, financial, legal, social, emotional, and psychological, as well as to subjects' privacy or confidentiality) may impact the rights, safety or well-being of subjects or others.

Office for Human Research Protection (OHRP) considers unanticipated problems, in general, to include any incident, experience, or outcome that meets **all** of the following criteria:

(1) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

(2) Related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

(3) Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognised.

Examples from OHRP Guidance (Appendix B)

(Appendix B) http://www.hhs.gov/ohrp/policy/AdvEvntGuid.pdf

(1) An investigator conducting behavioural research collects individually identifiable sensitive information about illicit drug use and other illegal behaviours by surveying college students. The data are stored on a

laptop computer without encryption, and the laptop computer is stolen from the investigator's car on the way home from work. This is an unanticipated problem that must be reported because the incident was (a) unexpected (i.e., the investigators did not anticipate the theft); (b) related to participation in the research; and (c) placed the subjects at a greater risk of psychological and social harm from the breach in confidentiality of the study data than was previously known or recognised.

(2) As a result of a processing error by a pharmacy technician, a subject enrolled in a multicentre clinical trial receives a dose of an experimental agent that is 10-times higher than the dose dictated by the IRB-approved protocol. While the dosing error increased the risk of toxic manifestations of the experimental agent, the subject experienced no detectable harm or adverse effect after an appropriate period of careful observation. Nevertheless, this constitutes an unanticipated problem for the institution where the dosing error occurred that must be reported to the IRB, appropriate institutional officials, and OHRP because the incident was (a) unexpected; (b) related to participation in the research; and (c) placed subject at a greater risk of physical harm than was previously known or recognised.

(3) Subjects with cancer are enrolled in a phase 2 clinical trial evaluating an investigational biologic product derived from human sera. After several subjects are enrolled and receive the investigational product, a study audit reveals that the investigational product administered to subjects was obtained from donors who were not appropriately screened and tested for several potential viral contaminants, including the human immunodeficiency virus and the hepatitis B virus. This constitutes an unanticipated problem that must be reported because the incident was (a) unexpected; (b) related to participation in the research; and (c) placed subjects and others at a greater risk of physical harm than was previously known or recognised.

Additional examples of reporting UPIRTSOs

- *General events* (non-medically-related)
    - A subject start crying (without self-control) during an interview while being asked about his/her experience during high school.
    - The research team conducting the interview fires a gun in the field.
    - There is a breach of confidentiality in which at least one piece of the research data (or more) is revealed to an unauthorised person(s).

- *Medically-related events* (Remark: in the UR system, reporting 'adverse events', such as a new occurrence of toxicity, will be reported as, 'Type 1'.)
    - A subject in a diabetes research protocol is having chest pain and signs of a heart attack and emergency assistance is being given; however, the CPR machine is not working.
    - After a prepared vaccine is administered, it is found that the vaccine in the trial has been contaminated due to a mistake during the preparation process.
    - While the research is being conducted, it is found that the research procedures or the testing equipment gives a false positive that is higher than anticipated, resulting in a further thorough examination and increased costs.

Appendix 7
Researcher Ethics and Practices by National Research Council of Thailand (NRCT)

1. Researchers must have academic and managerial honesty and integrity.

Researchers must be self-honest, and do not claim others' work as their own nor plagiarise. Credits and references must be given to the owners or sources of information. They must be honest when seeking research grants and fair with regard to deriving benefits from the research.

Guidance

1.1 Researchers must be honest with themselves and others.

- Researchers must retain honesty throughout the research procedures, from topic selection, participant selection, and implementation to application.
- Researchers must respect others by giving proper citations to the persons or sources of information.

1.2 Researchers must be honest when seeking grants.

- Researchers must present data and ideas in an open and straightforward manner in their proposals.
- Researchers must present their project with honesty by not applying for duplicate funding.

1.3 Researchers must be fair with regard to the benefits from the research.

- Researchers must fairly distribute shares of responsibility to all co-researchers.
- Researchers must present their work in a straightforward manner by not claiming others' work as their own.

2. Researchers must comply with the obligations made by their funding and affiliated agencies.

Researchers must comply with the obligations and agreements agreed upon by all parties. They shall dedicate time to their research to ensure maximum quality

and meet the schedule. They must hold a sense of responsibility in not abandoning the work halfway through the process.

2 Guidance

2.1 Researchers must be aware of their research obligations.

- Researchers must thoroughly study the terms and regulations set by the funding body.
- Researchers must comply with all the terms, rules and regulations.

2.2 Researchers must dedicate time to their research.

- Researchers must dedicate their knowledge, skills and time to their research to ensure quality and benefits.

2.3 Researchers must have a sense of responsibility for their research.

- Researchers must have a sense of responsibility for their research and not abandon work without sound reasons. They must submit their work within the schedule and not commit a breach of agreement that causes damage.
- Researchers must fulfil their duty in completing the Final Report to ensure that the benefits derived from the research will be of future use.

3. Researchers must possess substantial knowledge required by their field of research.

Researchers must possess substantial knowledge in their field of research, and knowledge or expertise related to the subject matter in order to produce research of good quality and prevent errors in analysis, interpretation, or conclusion, which may cause damage to the research.

Guidance

3.1 Researchers must possess substantial knowledge, expertise or experience related to the subject matter in order to produce research of good quality.

3.2 Researchers must retain the standard and quality of research in the particular field to prevent damage to academia.

4. Researchers must take responsibility for their research subjects, either living or non-living.

Researchers must proceed with great care and precision when conducting research involving humans, animals, plants, art, culture, resources and the environment. They must have a conscience and determination to conserve art, culture, resources and the environment.

Guidance

4.1 Human or animal subjects must be used only as a last resort.

4.2 Researchers must conduct their research with a conscience not to cause harm to humans, animals, plants, art, culture, resources and the environment.

4.3 Researchers must take responsibility for any consequences of the research on themselves, their research subjects or society.

5. Researchers must respect the human subjects' rights and dignity.

Researchers must not focus heavily on academic benefits to the extent of ignoring and disrespecting the dignity of their fellow human beings. They must explain the research objectives to the subjects without deception or coercion, and violation of personal rights.

Guidance

5.1 Researchers must respect the rights of the human subjects and obtain their consent before conducting the research.

5.2 Researchers must treat human and animal subjects with kindness. They must not focus heavily on academic benefits to the extent of causing conflict.

5.3 Researchers must protect the rights and confidentiality of the research subjects.

6. Researchers must have intellectual freedom without any bias in all steps of the research process.

Researchers must have intellectual freedom and be aware that personal or academic biases may result in distortion of the data and findings, causing damage to the research.

Guidance

6.1 Researchers must operate with intellectual freedom and not on the basis of personal considerations.

6.2 Researchers must conduct their research based on academic principles without any bias.

6.3 Researchers must present their findings truthfully without any intention of distortion in the hope to obtain personal gains or cause damage to others.

7. Researchers shall put their research to good use.

Researchers shall publish their research for academic and societal benefits. They shall not overextrapolate the findings and use their research in an unethical manner.

Guidance

1.1 Researchers shall have a sense of responsibility and thoroughness when publishing their research.

1.2 Researchers shall publish their research with the best interest of academia and society in mind. They shall not overstate the research for personal gains.

1.3 Researchers shall present their research truthfully and not extrapolate the findings without academic investigation and verification.

8. Researchers shall respect the academic views of others.

Researchers shall remain open-minded and willing to disclose the research data and methods, listen to the academic views and grounds of others and make revisions to the research.

Guidance

8.1 Researchers shall demonstrate good interpersonal skills, and be willing to exchange ideas and promote understanding of the research with peers and other academics.

8.2 Researchers shall listen to others, make revisions and present their work following constructive feedback in order to produce accurate knowledge and put the research to good use.

9. Researchers shall have a sense of responsibility for all levels of society.

Researchers shall have a commitment to dedicate their intellectual capacity to research for academic advancement and the best interest of society and humanity.

Guidance

9.1 Researchers shall consider their topic carefully and conduct the research with a commitment to dedicate their intellectual capacity to research for academic advancement and the best interests of their institution and society.

9.2 Researchers shall be responsible for producing academic works which will contribute to social improvement. They shall not conduct research that is against the law, peace and moral values upheld by society.

9.3 Researchers shall strive to increase their contribution and dedicate time and effort to foster new generations of researchers in the intellectual, mental and behavioural departments.

References

1. National Research Council of Thailand. National Policy and Guidelines for Human Research [*nayobāi hǣng chāt læ nǣothāng patibatkān wich̆ai nai manut*]; 2015.
2. Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. 64th WMA General Assembly, Fortaleza, Brazil, October 2013.
3. International Ethical Guidelines for Health-related Research Involving Humans. Fourth Edition. Geneva. Council for International Organizations of Medical Sciences (CIOMS); 2016.
4. Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. 64th WMA General Assembly, Fortaleza, Brazil, October 2013.
5. Examples of Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO), version 5.28.09 [cited 2021 Mar 24]. Available from: https://www.rochester.edu
6. ICH HARMONISED GUIDELINE INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R2) Current Step 4 version, dated 9 November 2016.
7. 45 CFR 46 (US Code of Federal Regulations. Title 45 Public Welfare Department of Health and Human Services Part 46 Protection of Human Subjects) 2018 requirement.
8. National Research Council of Thailand, Ministry of Science, Technology and Environment. Researcher Ethics and Practices by National Research Council of Thailand [*nǣothāng patibat c̆hanyābān nakwic̆hai saphā wic̆hai hǣng chāt*]; 1998.
9. Operational guidelines for ethics committees that review biomedical research [*nǣothāng kān̄damnœ̄n kān̄ samrap khana kammakān̄ dān̄ c̆hariyatham phū mīna thī thopthuān phic̆hārana kān̄suksā wic̆hai thāng chīwa wētchasāt*]. Geneva: World Health Organization; 2000.
10. Sueblinwong T, Mahaisavariya P, Panichkul S, editors. Forum for Ethical Review Committee in Thailand (FERCIT). Ethical Guidelines for Research on Human Subject in Thailand, 2007 [*nǣothāng c̆hariyatham kān̄tham wic̆hai nai khonnai prathēt Thai Phọ̄.Sọ̄. sọ̄ngphanhārọ̄ihāsip*].

11. Forum for Ethical Review Committee in Thailand (FERCIT). Guidelines for Adverse Event Report from the Achieving Guidance in Clinical Trial Safety Information among Stakeholder Seminar [nǣothāng patibatkān rāingān hetkān mai phưng prasong čhak kān prachum sammanā Achieving Guidance in Clinical Trial Safety Information among Stakeholder] Forum for Ethical Review Committee in Thailand (FERCIT) June 2011."

Glossary

Research

Research refers to systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Human Subject Research

Human subject research is research in which an investigator (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Clinical Trial/Study

According to ICH GCP, *clinical trial/study* refers to 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.

According to US FDA, *clinical trial* refers to any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration. The terms ‘research’, ‘clinical research’, ‘clinical study’, ‘study’, and ‘clinical investigation’ are deemed to be synonymous.

Clinical Trial

According to 45 CFR 46, *clinical trial* means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioural health-related outcomes.

Research Participant/ Human Subject

Human subject means a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

- Intervention includes both physical procedures by which data are gathered (for example, venepuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- Interaction includes communication or interpersonal contact between investigator and subject.
- Private information includes information about behaviour that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
- Private information must be individually identifiable in order for obtaining the information to constitute research involving human subjects.
- An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or is associated with the biospecimen.

Protocol

Protocol refers to a document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.

A protocol is the main document of a research proposal, research project or graduate thesis proposal.

A protocol must substantially include topics and details to allow for HEC to assess whether the research findings can answer the research questions with credible evidence and the research implementation is ethical.

- The ethical justification for undertaking health-related research involving humans is its scientific and social value (CIOMS Guideline 1)
- Risks to subjects are minimized:(i) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (ii) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes (45 CFR 46).

Protocol Amendment

Protocol amendment refers to a written description of a change(s) to or formal clarification of a protocol.

Confidentiality

Confidentiality refers to ethical and legal responsibilities of investigators and institutions to protect private information of the participants from unauthorised access, use, disclosure and modification under Personal Data Protection Act, BE 2562 (2019) and the regulations of secure storage from data damage or loss.

Investigators must indicate confidentiality protection methods in the subject information sheet.

Serious adverse event (SAE) or Serious Adverse Drug Reaction (Serious ADR)

Serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose:

- Results in death;
- Is life-threatening;
- Requires inpatient hospitalisation or prolongation of existing hospitalisation.
- Results in persistent or significant disability/incapacity;
- Is a congenital anomaly/birth defect; or
- Is an important medical event 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.

Unexpected Adverse Event

Unexpected adverse event refers to an adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational medicinal product/summary of product characteristics for an approved product).

Internal Adverse Event

Internal adverse event refers to an adverse event experienced by patients or participants enrolled in protocols conducted by RIHES regardless of regardless of the location of occurrence.

External Adverse Event

External adverse event refers to an adverse medical event occurring to patients or subjects of research in other institutions, both domestic and overseas.

Noncompliance

Noncompliance refers to any action or activity that fails to comply with RIHES regulations and announcements or internationally recognised research ethics guidelines (e.g. ICH GCP, Declaration of Helsinki and the) Medical Council Regulations)

Any failure to comply with the regulations that significantly affects the rights and safety of participants is deemed 'serious noncompliance'. HEC may temporarily suspend approval until the investigator makes changes or terminate approval.

Protocol Deviation/Violation

A *protocol deviation/violation* refers to an excursion from the protocol that is not implemented or intended as a systematic change.

1) **Major deviation** refers to any excursion that affects the participant's rights and safety, data reliability and/or the participants' intention of participating.
2) **Minor deviation** refers to any excursion that does not affect the participant's rights and safety, data reliability and/or the participants' intention of participating.

Deviations may result from investigators (e.g. specimens being submitted to the lab behind the schedule) or participants (e.g. not showing up at the follow-up appointment or forgetting to take the medications).

Any failure to comply with the regulations that has a major impact on the participant's rights and safety shall be deemed a serious noncompliance. HEC may temporarily suspend approval until the investigator makes changes or terminate approval.

Conflict of interest

Conflict of interest is a situation in which the investigator's personal interests compromise or bias professional judgment or duty as a researcher. The benefits may be financial (e.g. having shares in the company sponsoring the research) or non-financial. 'Conflict of interest', 'conflict in interest' and 'conflicted interest' are deemed synonymous.

Deception

Deception refers to any act of actively deceiving participants e.g. having someone pose as a patient or a user to study the behaviour of the service providers.

Withholding information

Withholding information refers to any act of withholding some information about the protocol from the participants to obtain scientific validity.

Unanticipated problem

Unanticipated problem refers to any incident, experience, or outcome that meets all of the following criteria: (A) unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; (B) related or possibly related to participation in the research; and suggests that the research places subjects or others at a greater risk of harm.

Unexpected adverse event

Unexpected adverse event refers to an unexpected or unanticipated event resulting from (1) the method, procedure or interaction during the research, (2) identifiable personal information collection, (3) the participant's existing illness, abnormality or condition and/or (4) other causes unrelated to the research or the participant's existing illness, abnormality or condition.

Suspected unexpected serious adverse reaction (SUSAR)

Suspected unexpected serious adverse reaction refers to any serious adverse reactions due to the medicines or research product administered in a clinical trial that is deemed unexpected by the sponsor.

HEC

HEC refers to the Human Experimentation Committee (HEC) which is comprised of members from scientific and non-scientific disciplines appointed by the Director of RIHES. It is responsible for the initial review and making a decision to approve, approve after revision or reject, and the continuing review by suspending or terminating approval if it is deemed to further implementation may cause harm to the rights, safety

and welfare of the participants, or the data reliability. This is to protect the rights, safety and welfare of the participants.