Guidelines for Researchers

In Conducting Research Involving Human

by

Human Experimentation Committee (HEC)

Version 5.1

2026

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Guidelines for Researchers
in conducting research involving human

By Human Experimentation Committee (HEC)
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Contact: Office of Research Ethics (ORE)
Research Institute for Health Sciences (RIHES), Chiang Mai University
Tel 0-5393-6148, Ext 360

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 studies 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, identifiable private information, 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 research involving human protocol conducted and/or co-conducted by RIHES; protocols by another institution that are requested to be conducted at RIHES; and protocols by other CMU organizations that have MOUs with RIHES.

The Working Party for Establishing the Standard Procedure for the Human Experimentation Committee, RIHES has created these guidelines on the approval process and research involving human protocol preparation to provide basic ethical knowledge and to employ them as the guidelines for researchers to prepare documents for approval from the HEC. These guidelines have been revised from the 2024 editions. It is hoped that they will be of use to researchers as a research manual for ethics application.

Note that in this Guideline, researchers and investigators are synonymous.

The Working Party for Establishing the Standard Procedure
for the Human Experimentation Committee
January 2026

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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 with research involving human, 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 research involving human 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 Code of Federal Regulations 45 CFR 46, as stated above. The Office for Human Research Protections (OHRP), DHHS is responsible for operations related to FWA to ensure that research participants 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.

HEC's operation had been internationally certified by WHO-TDR-SIDCER (The Strategic Initiative for Developing Capacity for Ethical Review) in partnership with FERCAP (Forum for Ethical Review Committees in the Asian and Western Pacific Region) for the first time in 2008, followed by periodically reviewed and certified in 2011, 2015, 2019, and 2023 respectively. Inspection visits and performance assessments are conducted consistently to provide assurance for funding bodies, researchers, and journals.

Moreover, RIHES HEC is also an ethics committee that is accepted by the Food and Drug Administration (FDA), Thailand and has been renewed the acceptance as an ethic committee for considering drug-related clinical research per the letter of acceptance no. 09/2023.

1.3 Research Institute for Health Sciences Responsibilities

The RIHES's responsibilities are as follows:

1.3.1 Appoint an HEC to review protocols in both scientific and ethical aspects, and approve protocols, as well as support HEC's operation to ensure fairness and independence from interference;

1.3.2 Protect the rights and welfare of the participants by requiring the researchers to present their research involving human protocols to HEC for approval – the researchers 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 prior to implementation;

1.3.3 Provide HEC with sufficient resources such as meeting locations, document storage, administrative personnel, and office equipment;

1.3.4 Encourage HEC to participate in research ethics training for improved capacity in reviewing the research protocol; and

1.3.5 Promote cooperation between local, national, and regional human research ethics committees to create a network of information exchange.

1.4 Human Research Ethics Committee Responsibilities

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

1.4.1 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 prevention of possible harm to the participants in a particular protocol.

1.4.2 Review research protocols in terms of scientific and ethics basis, including suitability of the researchers, equipment, location, as well as materials and methods used in obtaining an informed consent;

1.4.3 Review the study documents/amendment from the initial submission and continue reviewing until the study completion;

1.4.4 Authorized to approve or disapprove a research study, amendment or study extension until the study completes;

1.4.5 As for approved protocol, the committee are authorized to withhold approval or revoke previously given approval if violation of regulations and requirements

are found during continuing review, or the study causes seriously unexpected harms to research participants;

1.4.6 Authorized for other duties as specified in the standard operating procedure of the Human Experimentation Committee;

Alternate members bear the responsibilities and authorization as follows:

1.4.7 Primary reviewers on behalf of the regular member who are unable to attend the meeting.

1.4.8 Attend the meeting to complete the quorum when a regular member leaves or is absent from the meeting.

1.4.9 Attend the meeting to as an observer.

Only items 1.4.7-1.4.8 can be made by the Alternate members as regular member and can vote at the meeting.

1.4.10 Independent consultants bear the responsibilities and authorization as follows Give opinions on the research project according to the issues that the committee has consulted but cannot vote on the decision.

1.5 Ethical Principles and guidelines for research involving human

Human research must be conducted based on ethical principles which are widely known and implemented as references per the followings.

1.5.1 The World Medical Association's Declaration of Helsinki is considered the first international code of ethics published in 1964, and has been consistently revised with 2024 edition as the latest one. It is stated to be applied by physicians for research studies, but can also be used in a wider scale. It has been used along with other 2 international ethical principles; ICH GCP and CIOMS Ethical Guideline.

1.5.2. ICH Good Clinical Practice Guideline (ICH GCP E6) which is applied to investigational new drug or new biological objects to diagnose, prevent, or treat diseases. Its outstanding focuses covering right protection, safety and well-being of subjects with quality system which enhances reliable research results. It is widely used as reference and recommended in researchers' training. The revision is made as the E6(R3) edition, the latest version, in 2025

1.5.3. CIOMS Ethical Guidelines, with full name of latest revised edition as Ethical guidelines for health-related research involving humans in 2016, consists of guidelines with topics covering currently conducted health research studies, including research using personal information and biological materials.

1.5.4 Handbook of the National Policy on Ethics Oversight and Ethical Guidelines for Research Involving Humans. August 2025. The National Research Council of Thailand.

In the Unites States, the National Research Act was created after a scandal over unethical syphilis studies in 1972 which led to the appointment of The National Commission for the Protection of Human Subjects of Research ("The Commission") to be responsible for finding basic ethical principles of biomedical and behavioural sciences research studies. The Commission has reported 3 basic ethical principles called The Belmont report: Ethical principles and guidelines for the Protection of Human Subjects of Research in 1979 as follows.

1. Respect for person: As a person have autonomy; the ability to reflect and make decision independently, requesting him/her to participate in a research study requires an informed consent by (1) providing sufficient information to support decision-making (information) (2) providing comprehensive information (comprehension) and (3) allowing voluntary decision making (voluntariness) without coercion (coercion) or excessive temptation (undue influence).

People with impair decision-making ability due to physical or intellectual condition, or are in an environment with limitation for decision making should receive more protection. Those are often referred to as vulnerable participants.

2. Beneficence: Two general rules of beneficence include (1) cause no harm, and (2) must maximize benefits and minimize potential risks.

Complying with this principle is achieved through a systematic and substantial assessment of risks and benefits, focusing on the risks and benefits of research participants. The benefits and risks must also be "balanced" in a "satisfactory ratio."

3 . Justice: The justice is referred to as fair distribution of risks and burdens (distributive justice) with fairness in terms of both methods and result of participant recruitment. The analysis of recruitment method should not be biased by gender, race, financial status (poor or rich), but factors that will answer research questions. It also includes the protection of vulnerable groups such as poor participants, children from foster home, ethnic minorities, inmates, psychiatric patients or people with limited access to health services. These groups of people should not be enrolled on the ground of easy recruitment and management, or for the benefit of more privileged group.

The basic ethical principles are an important factor used by the US Federal Government to improve the regulations of the Federal Policy for Protection of Human Subjects, or also known as the Common Rule which is applied to 19 government agencies. It was revised in 2017, effective in 2018, so-called 2018 Common Rule. As for health researches, it is also governed by Department of Health and Human Services (DHHS)

regulations 45 CFR Part 46 with subparts for the protection of pregnant women and fetuses (Subpart B), prisoners (Subpart C), and children (Subpart D).

The basic ethical principles are addressed in many countries worldwide. They are considered an important part that researchers must learn in combination with Common Rule and 45 CFR 46 in the Human subject protection training.

Chapter 2
Researcher's Guidelines

2.1 Definition of Research involving human

Research involving human is a 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, analyses, or generates identifiable private information or identifiable biospecimens.

Research involving human 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

2.2.1 All principal researchers and co-researcher must complete a 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. Researchers must attend the Human Subject Protection training, which is a part of the CITI Programme (https://about.citiprogram.org/), or any other training programmes organised by any universities or organisations of which the contents cover Basic ethical principles, Federal Policy for Protection of Human Subjects and 45 C.F.R Part 46 Subparts, IRB roles in protection of human research participants, IRB review, Informed consent process for research, Assessment of risk and benefits, Exempt/Non-exempt Human Subject Research, The HHS Office for Human Research Protections (OHRP), Federalwide Assurances based on (https://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-training/human-research-protection-foundational-training/index.html) This includes the Human Subject Protection & Good Clinical Practice training course, Human Subject Protection (HSP) by NECAST, National Research Council of Thailand (NRCT)

and Ministry of higher education, science, research and innovation (https://elearning-necast.nrct.go.th/).

B. Researchers conducting Clinical Trial of drugs, biological products, medical devices, dietary supplements, or other products regulated by Thai FDA must attend a good 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) e.g. GCP online of Thammasat University (https://www.med-tu.org/GCP/)

** All researchers and co- researchers have signed, certified and dated the evidence of completion.

2.2.2 Researchers should follow the following principles/guideline:

A. The Declaration of Helsinki
B. The Belmont Report
C. The ICH GCP
D. Handbook of the National Policy on Ethics Oversight and Ethical Guidelines for Research Involving Humans

2.2.3 All Principal researchers and co- researchers must disclose any conflict of interest in the protocol, especially financial ones.

2.2.4 Researchers must obtain a Certificate of Approval (CoA) from HEC prior to the study implementation.

2.2.5 After the CoA has been received, researchers must implement the study per the approved context as submitted. Any amendment to the protocol must be approved by the committee before implementation unless such amendment is done with urgency to protect the welfare of the participants.

Any action as described above done prior to approval to protect participants*'* safety *must be reported within three working days, including a prevention plan for the future. If the study or consent documents need to be revised, the amendment must be submitted for approval.*

2.2.6 As for the study approved in the HEC meeting (Full board review), the researchers must submit a progress report **in a frequency** as specified by the HEC. Progress report should be submitted as early as 45 days before the expiration date as indicated on the CoA together, with a copy of the CoA/memorandum indicating the expiration date enclosed.

A. If the review take place at the convened meeting within 30 days before HEC approval period expires, the HEC will retain the anniversary of the expiration date of the initial HEC approval.
B. In cases where the convened meeting is held more than 30 days before the initial HEC approval period expires, the HEC will consider granting

the renewal effective from the date of the meeting at which approval is given.

C. If 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. Researchers should not accept participants after the expiration date and should temporarily halt research activities, except ones that are necessary for the participants' safety, until they receive the HEC's renewal approval.

D. In cases where the research project fails to submit a progress report after receiving two reminder letters from the Office of Research Ethics, the investigator must submit the required documents to request project closure. Failure to do so will result in the investigator being ineligible to submit a new project for review.

E. In cases where the CoA has expired and renewal has not yet been granted, the investigator must suspend the enrolment of new research participants and temporarily halt all research activities, unless approval is obtained from the Chair of the Human Experimentation Committee to carry out certain activities deemed necessary for the best interests of the research participants.

2.2.7 For research projects approved under Expedited Review, the Certificate of Ethical Clearance is valid for one year or for the duration specified in the protocol If the study has not been completed within this period, the investigator must submit an official memorandum requesting renewal of the certification, indicating the current status of the research project, prior to the expiration of the certificate. A copy of the CoA or memorandum specifying the expiration date must also be attached. The renewal period will be granted effective from the original expiration date and the HEC will use expedited review procedure.

2.2.8 For protocols filing for exemption

If the study has low risk and there is no cause for reviewing the report, the researchers do not need to submit a Progress Report. The study close-out report must be submitted within 3 months after the study completion.

2.2.9 For clinical trials of drugs and biologics, e.g., vaccine, researcher must report:

A. Any internal SAE taking place within RIHES that causes death or is life-threatening to the participants must be reported to the HEC Chair by the principal investigator in writing within 24 hours after being informed. In 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 local or internal suspected unexpected serious adverse reaction (SUSAR) that causes death or is life-threatening to the participants must be reported to the HEC within 7 calendar days after the sponsor has confirmed the SUSAR or after the investigator is informed about the event. In case of an incomplete preliminary report, a complete report shall be submitted within 8 subsequent calendar days and a follow-up report within 15 calendar days.

C. Any local or internal suspected unexpected serious adverse reaction (SUSAR) that is non-fatal or not life-threatening to the study participants must be submitted to the HEC within 15 calendar days after the sponsor has confirmed the SUSAR or after the investigator is informed about the event. 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 non-local serious adverse event (SAE) that may increase the risk to the participants must be promptly report to the HEC Chair by the principal investigator within 15 calendar days after being informed, using CIOMS report or other standard report with sufficient information enclosed.

E. Any non-local SUSAR using the CIOMS Report or other standard report with sufficient information within the required period of their study or required by the research sponsor, or every six months but no more than a year (periodic or annual safety report)

F. The Safety Report by Data Safety Monitoring Board (DSMB)
   - The sponsor must report any significant change that increases the risk to the participants 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.

G. The Safety Information of the Research Product (Investigator's brochure/package insert), reporting non- SAE/SUSAR UAP of each individual with details of event and provided solution.

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

researchers 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)

2.2.10 Researchers 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.

2.2.11 Researchers or sponsors must report premature termination or temporary suspension within 15 calendar days along with a proposed follow-up treatment plan for the participants.

2.2.12 Researchers must submit their study close out Report within 3 months after the study completion with research conclusions, except for a multicentre study in which RIHES is the only research site, in which case the study closure can be reported at RIHES without having to submit the research conclusions.

2.2.13 Researchers shall comply with the Researcher Ethics and Practices by the National Research Council of Thailand (NRCT).

2.3 Submission for Review

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

2.3.1 Submission for *exemption from Ethical Review* applies to research with very minimal risk that only causes inconvenience and meets the criteria and lists in **Appendix 1**. The HEC will issue a Certificate of Exemption without the researchers having to submit a Progress Report. However, any amendment in the study must be submitted for approval. The study close out report must also be submitted once the study is complete with study results within 3 months after the study completion. The exemption review will be 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.

2.3.2 Submission for expedited review applies to a study research with minimal risk that meets the criteria and lists in **Appendix 2**. HEC secretary will propose the HEC Chair or two members to review and present the reviewed result to the Chair. The HEC Chair will issue the CERTIFICATE OF ETHICAL CLEARANCE. The

process from receiving the complete documents until consideration result is issued takes 10 working days. By the way, expedited review only applies to amendment submission with 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.

2.3.3 *Convened review* applies a research study with greater than minimal risk. HEC secretary will propose the HEC Chair to appoint no more than three members to review and present the reviewed result to the Chair. The HEC Chair will issue the CERTIFICATE OF ETHICAL CLEARANCE. The process from receiving the complete documents until consideration result is issued takes 30 working days. By the way, convened review only applies to resubmitted protocol submission,
other reports that meet the criteria (See Appendix 3), Serious Adverse Event; SAE, Suspected Unexpected Serious Adverse Reaction; SUSAR), DSMB report, progress report and deviation/violation report.

The HEC convened meeting normally takes place once a month. The staff of the Office of Research Ethics will notify the researchers and coordinators of the schedule of the annual meeting plan in advance by email and post on the Office of Research Ethics website https://www.rihes.cmu.ac.th/ias/ore/. The submission window for each meeting may change from the annual meeting plan. The Office shall announce any changes via e-mail notifications.

2.4 Preparing Documents for Submission

researchers must submit the Form for Ethical Approval to the HEC Chair and enclose with a list of documents by the category of review. Relevant notes and various forms are available at https://www.rihes.cmu.ac.th/ias/ore/

2.4.1 Initial submitted Protocols

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

	Document List	Form
[ ]	Full Research Protocol in Thai or English, specify version and date.	
[ ]	Biographies of the principal researchers and co- researchers that are current, certified and signed with a date	
[ ]	Declaration of Conflict of Interest: Everyone in the study listed on the research team in the project must fill in and sign/date	**HEC F55**
[ ]	Initial Review Submission Form	**HEC F29**
[ ]	Initial Review Application Form	**HEC F30**
[ ]	Informed consent documents, consisting of • Patient or Subject Information Sheet, and	

	• 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-researcher from another RIHES department/agency, or another external agency (if applicable)	
[ ]	Certificate of Indemnity or Insurance for compensation in case of patient's or participant's sickness due to research participation (in case the sponsor is a private funding body and the research is a product research)	
[ ]	Material Transfer Agreement (if applicable)	

* In case there is 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 Resubmitted study revised documents per HEC recommendations to be reviewed in a convened meeting

Three hard copies and one electronic copy 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 Modifications required prior to its approval/favorable opinion

2 sets of documents (1 original and 1 copy) and one electronic copy are required for submission.

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

2.4.4 Protocols Amendments after approval

For the protocol amendments with major changes which require full board review, submit 2 sets of documents (1 original and 1 copy) and one electronic copy.

For the protocol amendment with minor changes which require an expedited review, submit 1 set of documents (original).

	Document List	Form
[ ]	Protocol Amendment Review Form	**HEC F37.1**
[ ]	Summary of Changes for Additional Changes/Revisions per HEC's recommendations	**HEC F36**
[ ]	Revised documents/requesting additional review, track-change version	
[ ]	Revised document/requesting additional review, clean version with new version number and date assigned	
[ ]	Other relevant documents	

2.4.5 Progress report/continuing review report

2 sets of documents (1 original and 1 copy) and one electronic copy are required for submission.

	Document List	Form
[ ]	Current research protocol	
[ ]	Progress Report Form	**HEC F38.1**
[ ]	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 Close out study report

2 sets of documents (1 original and 1 copy) and one electronic copy are required for submission.

	Document List	Form
[ ]	Close-out study report	**HEC F39.1**
[ ]	Other relevant documents (if any)	

2.4.7 Premature termination or suspension of a study report

2 sets of documents (1 original and 1 copy) and one electronic copy are required for submission.

	Document List	Form
[ ]	Report Form for Premature Termination or Suspension	**HEC F43.1**
[ ]	Other relevant documents e.g. reports by DMSB or sponsors (if any)	

2.4.8 Safety Report

A. Report on Local SAEs/SUSARs or unanticipated problems (UAPs)

B. *2 sets of documents (1 original and 1 copy) and one electronic copy are required for submission.*

	Document List	Form
[ ]	Internal SAE/SUSAR/UAP Report Form	**HEC F44.1**
[ ]	External SAE/SUSAR/UAP Report Form	
[ ]	DSMB Report	**HEC F56.1**
[ ]	Safety Information of investigational Product (Investigator's brochure/Package Insert)	**HEC F56.1**
[ ]	Other documents:	

For reporting a single case, use Form *HEC F44.1*, the CIOMS Form or other standard forms with sufficient information as follows:

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) Other medications not from the study
7) Event
8) Results of event (severity)
9) 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.

C. Report on internal SAEs occurring <u>at</u> RIHES

2 sets of documents (1 original and 1 copy) and one electronic copy are required for submission.

The principal investigator shall submit a written report to the HEC Chair within 24 hours (in case of deaths or life-threatening events) of being informed, or seven calendar days (in case of non-fatal or non-life-threatening events) of being informed. Use Form *HEC F44.1*, the CIOMS Form or other standard forms sufficiently covering the same information.

D. Report on Internal SUSARs/UAPs occurring at RIHES

2 sets of documents (1 original and 1 copy) and one electronic copy 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 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 F44.1*, the CIOMS Form or other standard forms sufficiently covering the same information.

E. Report on external SAEs occurring outside RIHES

2 sets of documents (1 original and 1 copy) and one electronic copy 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 participants) of being informed, using the CIOMS Form or other standard forms sufficiently covering the same information.

F. Report on external SUSARs/UAPs occurring outside RIHES

2 sets of documents (1 original and 1 copy) and one electronic copy 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.

G. DSMB Report using Form *HEC F56.1*

- The sponsor shall report any significant change that results in the increase of risk to participants and new issues that negatively impact the safety of the

participants 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.

H. Safety information of Research Product (Investigator's brochure/Package Insert) using Form *HEC F56.1*

I. Report on local or internal AEs occurring at RIHES

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.

2.4.9 Submitting other documents

Other documents not mentioned in the above lists such as protocol team's reports, newsletters, thank you letter to participants and others

Two sets of documents (one original and one copy) and one electronic copy 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 initial submitted version should be labelled 'Version 1.0' and for each amendment, the number shall increase accordingly.

2.6 Submission Location

Researchers submit the hard copies of the documents at the Office of Research Ethics (ORE), on the third floor, Room 03-020/00, and the documents will be checked against the requirements. The checking officer shall notify the investigator If any documents are incomplete/inaccurate. Once all documents are complete/accurate, 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 via email rihes.hec@gmail.com.

2.7 Notification of Result

For exemption review, ORE officers will notify the review result and issue the Thai and English version of CERTIFICATE OF EXEMPTION to the researcher for further acknowledgment, not more than 5 working days after the HEC secretary proof the exemption criteria and the HEC chair decide whether the research protocol follows the exemption criteria or not.

For expedited review, ORE officers will notify the official result signed by the HEC Chair within 5 working days after receiving the review result from the committee.

For convened review, 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. The official result shall be notified within 10 working days after the meeting according to the RIHES administrative protocol.

2.8 Certificate of Approval (CoA) Renewal

Researchers must apply for renewal of their certification and should submit a progress report within 45 days prior to the expiration date. The HEC Secretary will send a letter notifying researchers twice: the first time: 60 days before the expiration date, the second time: 45 days before the expiration date. The starting date for the renewal are mentioned in Sections 2.2.6 and 2.2.7.

In case the CoA has expired and the renewal document has not been received. The researchers will not be able to enroll new study participants and must temporarily suspend the research unless approved by the HEC Chair to proceed with certain activities in the best interest of the study participants.

2.9 Resubmission of study amendment with major changes

As for resubmission per the committee's recommendation with major changes, the resubmission should be made within 2 months from the date RIHES administrative officers received and stamped the official letter of the HEC. If it's overdue, the proposal must be handed in as the initial submission, except that the researcher proposes to extend the time period for submitting research project documents to the HEC. The HEC Chair will consider the request.

2.10 Close out report (Within scheduled timeline)

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

2.10.1 The number of enrolled participants is according to the study plan, and the HEC-approved research activities are completed.

2.10.2 The collection, use and analysis of identifiable data are complete and data or tissue samples are no longer collected from the participants. No request of secondary use of biospecimens from a specimen repository.

2.10.3 Industry-sponsored study has an official “Close-out letter” from the sponsor.

2.11 Storage of Relevant Documents

As for investigator-initiated research, research documents shall be stored for at least five years or as indicated by RIHES or the sponsor regulations (if any), and then destroyed using accepted methods.

2.11.1 Paper documents shall be destroyed using a shredder.

2.11.2 Computer files shall be deleted permanently from the hard disk or zipped with a password for unzipping and stored in a password-protected personal computer.

As for pharmaceutical-sponsored drug trial, the regulations of the sponsor shall be followed.

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. Similarly, if the Research Ethics Committee, Faculty of Medicine has considered and approved the protocol. HEC will not re-review. It is considered only one party. This criterion applies exclusively to research projects of RIHES with personnel under the Faculty of Medicine as the PI or as a co-investigator and research projects of personnel under the Faculty of Medicine with personnel under RIHES as co- researchers. Researchers of protocols that meet this criterion shall proceed as follows.

2.12.1 Submit the Initial Review Submission Form and relevant documents to only one EC. For example: submit to HEC and once the protocol is approved, Researchers 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.

2.12.2 Any amendment/Progress Reports/other reports shall be submitted in the same manner as in no 1.

2.12.3 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: Researchers 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 Applied research on educational evaluation methods in the areas of cognitive, diagnostic, aptitude, and achievement. The research uses survey and interview methods that must :

(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) Cause damage to the reputation of the informant organisation by the publication of the survey results;

(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 researchers;

(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 researchers 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 Research using laboratory-grown microorganisms or parasites, or research using microbial or parasite specimens isolated from clinical specimens with no link to identifiable personal information

2.8 Laboratory research using samples from commercial service agency such as research using cell lines purchased from ATCC or requested from other laboratories by complying with the Material Transfer Agreement (if any)

2.9 Research using samples from the skeleton or soft cadaver from the Faculty of Medicine, or a research using samples from the skeleton or soft cadaver from the Faculty of Medicine who has documents to surrender his/her body for research

2.10 Research using samples from the teeth that were removed from regular dental work.

2.11 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.

2.12 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 the prisoners, HIV-infected individuals, adolescent mothers, marginalized people (stateless persons, foreigners, refugees or asylum seekers, homeless people, and human *in vitro* fertilization.

(2) Research related to behavior or attitude of which the results potentially lead to speculation about the identity of a group of individuals or a community, and may cause damage to reputation or lead to lawsuit;

(3) Surveys, interviews, and group discussions with children, although no personal information is recorded.

Appendix 2
Types of Activities and Research Eligible for Expedited review

1. 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.
2. 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 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 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.
3. Research that involves a non-invasive collection of biospecimens (e.g. fluid and excrement collection or nail clippings in a non-disfiguring manner).
4. 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.
5. 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).
6. Research using biological samples obtained from previous research which have been stored in a repository with broad consent and appropriate governance.
7. Research that involves personal traits or groups of individuals, or uses surveys, interviews, history taking or focus groups, and recording data that can directly identify individuals or through coded connections.
8. Collection of audio, video, digital data and photos for research purpose.
9. Research operation to eliminate immediate hazards for the safety of research participants.
10. Research related to benign behavioral intervention combined with the collection of data from adult research participants by answering verbal or written questions,

including data collection by visual and audio recordings, which the research participants have agreed to in advance and meet at least one of the following criteria:

1) The data to be collected is recorded by the investigator in such a way that it is not possible to directly identify the participant or through an identifier linked to the participant.

2) Disclosure of any of the research participants' answers to the outside world will not create a risk of criminal or civil liability or damage to their financial position. employment, educational advancement, or reputation, or

3) The data to be collected is recorded by the researcher in such a way that it is not possible to identify the participant directly or through an indicator linked to the participant.

11. Establishment of biological sample/research data inventory by using broad consent for future research.
12. Protocol amendments are minor changes to approved protocol that result in an increase in the risk of participants not greater than minimal risk or do not significantly change the risk/benefit balance assessment (non-significant risk), such as:

    1) Correction of Mistakes Correction of writing styles that retain the original meaning

    2) Changing the co-investigator's contact address.

    3) Change of project manager without causing a change in areas of expertise.

    4) Request for an increase in the amount of blood collected because the original volume is not sufficient for analysis, etc., However, this excludes genetic testing and the translated informed consent forms in Foreign Languages.
13. The progress report of the research studies with initial submission approved via expedited review in which some of them are requested by the HEC Chair or the committee to submit the progress report.
14. 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.
15. DMSB reports indicating no changes in the safety data that affect participants.
16. Revised safety information of research products (investigator’s brochures/package inserts).
17. Adverse Event or IND Safety Reports that have undergone review but are resubmitted by researchers from another institution due to the protocol being a multi-centre research.

Remark: *For item 10. research using harmless behavioral interventions must be short-lived, non-harmful, non-painful, non-disgusting or humiliating, non-invasive, and not have a significant long-term negative impact. Examples of harmless behavioral interventions include having participants play online games, having participants play puzzle games in*

a noisy environment, or having participants decide how to allocate nominal cash to themselves and others.

Expedited review does not apply to a protocol which:

(a) The circumstances or health vulnerabilities of the research participants make it anticipated that the low-risk methods listed above may pose a risk exceeding the low risk.

(b) The disclosure of participants' responses poses a risk of civil or criminal liability, or negatively impacts their financial status, employment, insurance, or career, or leads to stigmatization, unless the research project has demonstrated adequate measures to protect against invasion of privacy and confidentiality so that the risk is no more than minimal.

(c) The reporting of research results is likely to predict the identities of groups of people or communities and may lead to reputational damage or legal action.

Appendix 3
Types of Protocol Changes

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 major and minor changes

Major or substantial change	Minor or non-substantial change
Document • There are new study documents to be distributed or given to study participants with different content from the previous committee-approve version. • There are changes in any study documents to be distributed or given to study participants. • There are changes in the insurance conditions for compensation from injuries. • There are added sensitive content in a questionnaire, interview or additional new documents.	**Document** • There are new study documents to be distributed to study participants with similar content from the previous committee-approve version. • There are changes in writing pattern but the same meaning maintained. • There are minor edits in participant information sheet such as correcting typos or paraphrasing sentences to make them easier to understand. • There are renewed injury insurance documents with the same sum insured. • There are minor edits in study documents such as survey, questionnaire, interview or brochure with no sensitive content.

Major or substantial change	Minor or non-substantial change
	• There are paraphrased contents in the study documents without changing their meaning. • There are translations of the approved documents. • The recruitment documents are produced per the approved methods.
Research team • There are changes in principle researchers or main coordinators.	**Research team** • There are changes in co- researchers in research personnel. • There are change in research study executives.
Study method • Any procedure exceeding minimal risk per the faculty announcement is added. • Procedure specified in the protocol is canceled. • More procedures for participants are significantly added. • There are changes in drugs/investigational drugs - Change in medication usage pattern such as from oral intake to injection - Change in doses - Change in duration of the medication - Change in comparative drugs - Change in the list of prohibited concomitant drugs	**Study method** • The amount of collected blood is slightly increased since the previously specified amount is insufficiency for analysis. • The frequency or quantity of biological samples is decreased as long as the risk/benefit ratio is not affected.
Study protocol • The study objectives are changed. • The study endpoint is changed and affected the participant safety. • The target population is increased.	**Study protocol** • The study name or code is changed. • There are minor modifications to the recruitment process.

Major or substantial change	Minor or non-substantial change
• The participant compensation is so highly increased that it seems like an improper inducement, or so largely decreased that it seems like participant exploitation. • The controlled group or placebo group is increased or canceled. • The inclusion/exclusion criteria is changed, affecting risk/benefit ratio. • The recruitment methods are changed, affecting potential participant's confidentiality or might be consider threatening, or participant might feel considerate towards study staff. • The study sponsors are changed. • There are supplementary studies from the main study such as - Pharmacokinetics or pharmacogenetics sub-study. - genetic testing or new genetic testing methods are added. - Tissue samples are stored in repository for genetic testing. • The total number of target participants from all study sites is changed. - Increase at least 5 more participants from the previous plan of 20 participants - Increase 20% more from the previous plan of more than 20 participants - Reduce the target number to the point that might affect the answers to the research question -	• The new study site is added in a multicenter study • The number of target participants on a particular site is increased/decreased without affecting the total number of target participants from all sites (For a multi-center study) • The methods for delivering and storing biological samples are changed. • Contact information of researchers or medical director is changed. • The study signatory is changed. • The recruitment period is extended along with the changing study duration. • The study duration is extended due to ongoing data analysis or other activities without new recruitment.

Major or substantial change	Minor or non-substantial change
Monitoring • Members of Independent Data and Monitoring Committee (IDMC) are increased or decreased. • Clinical examinations, biological examinations and study visits are increased or decreased. • Monitoring visits are decreased.	**Monitoring** • Members of Independent Data and Monitoring Committee (IDMC) are changed.
Investigator's Brochure • There are changes in clinical data which affect the followings. ○ Safety of research participants ○ and/or Safety of the research study ○ and/or assessment of expectedness of a suspected serious adverse effect, referred by IB.	**Investigator's Brochure** • The safety information in the IB are changed with prior notification to the committee without affecting the information in the information sheet and informed consent documents.

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, researchers must give one copy of the documents to participants.

Signing the informed consent form is the standard protocol but, in some cases, researchers 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 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 researchers 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 or 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 case of inquiry regarding participant rights, storage and use of identifiable private information or biospecimens, or the contact person In case of harm occurring because of research participation.

Researchers should study further about the Common rules, CIOMS guideline and GCP.

Informed Consent Documents

In case informed consent documents presented in great length such as in clinical trials, researchers 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

Researchers should have a separate set of the main informed consent documents as shown in the main research objectives. As for 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.

The sample collection might be included in the main consent form only for non-clinical-trials.

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 [*nǣothāṅ læ tonbæp̄ ʻēkkasān̄ khọ̄mūn̄ læ khọ̄ khwām yinyọ̄m samrap kān̄wicȟai thāṅ khlinik nai prathēt̄ Thai*]. Forum for Ethical Review Committee in Thailand; 2020.

Signing the Informed Consent Form

1. Participants 18 years old and over 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. If participants age over 7, but not exceed 18, assent and parental consent are required.
   3.1 If participants 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 If participants age 7 to less than 13, the Information Sheet for children must be separate from the one for parents.
   3.3 If participants age less than 7, researchers 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.

Researchers 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.
3. Signing document is not cultural norm of the community.

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

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

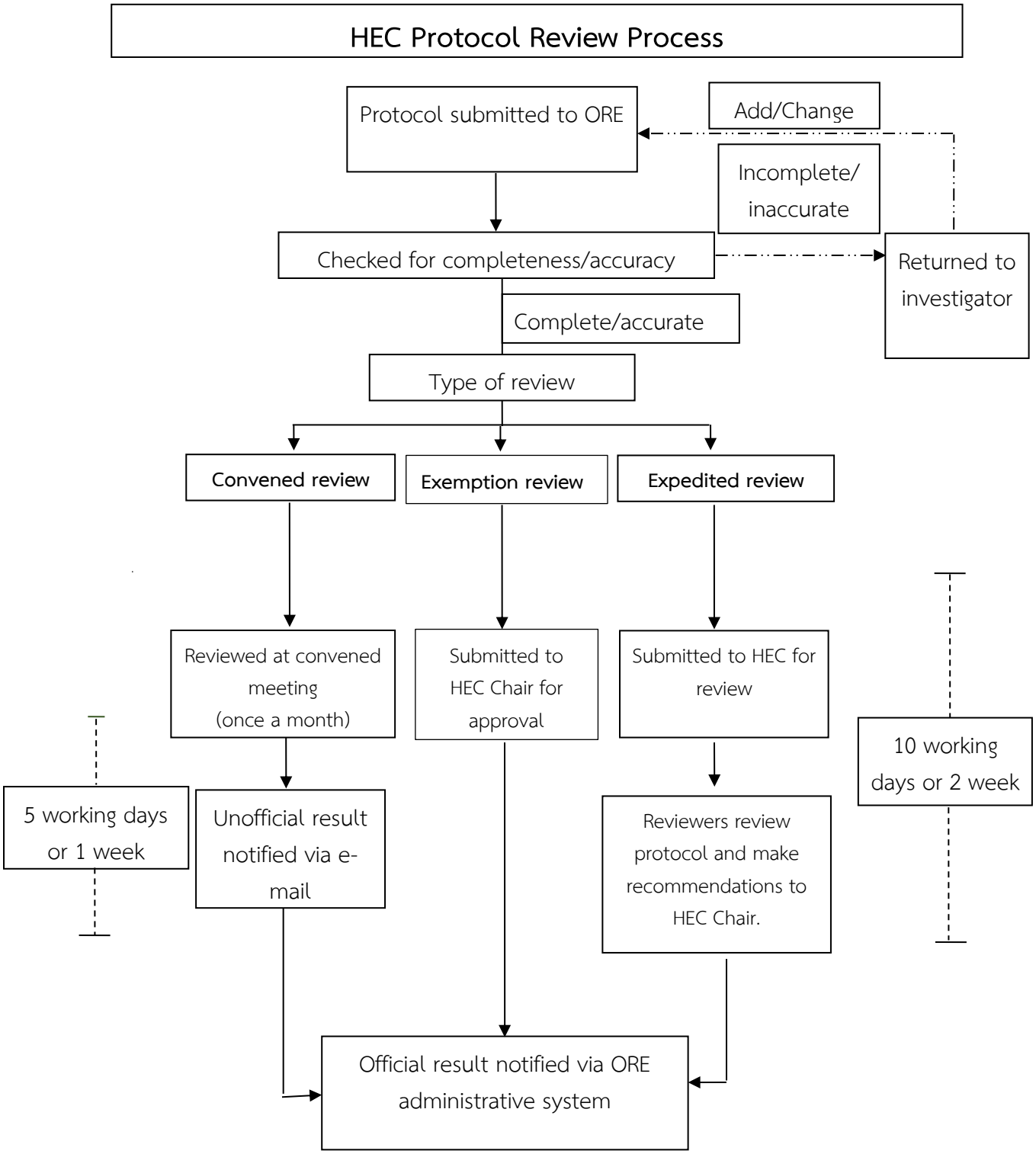
1. The research presents no more than minimal risk to participants
2. Waiving the informed consent procedure, or giving partial or modified information does not affect the rights and welfare of participants.
3. The research cannot be conducted without waiving the informed consent procedure, or giving partial or modified information, and
4. There is a plan to disclose information about the research except justified by a reason;

Note: Waiver of informed consent may apply to a survey or interview where investigate returning the answer implies consent by action.

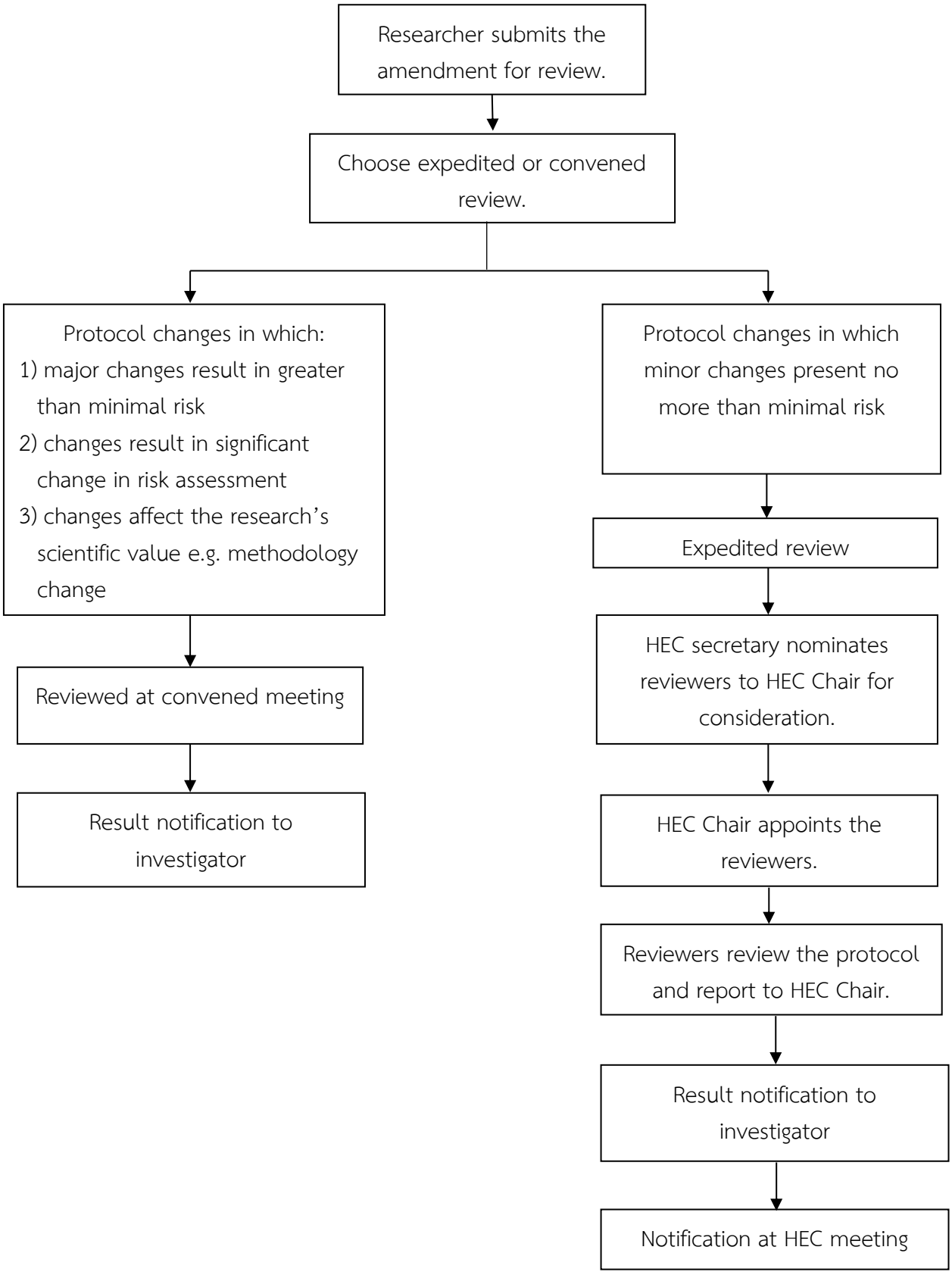
Appendix 5

Flow Chart for Protocol Review

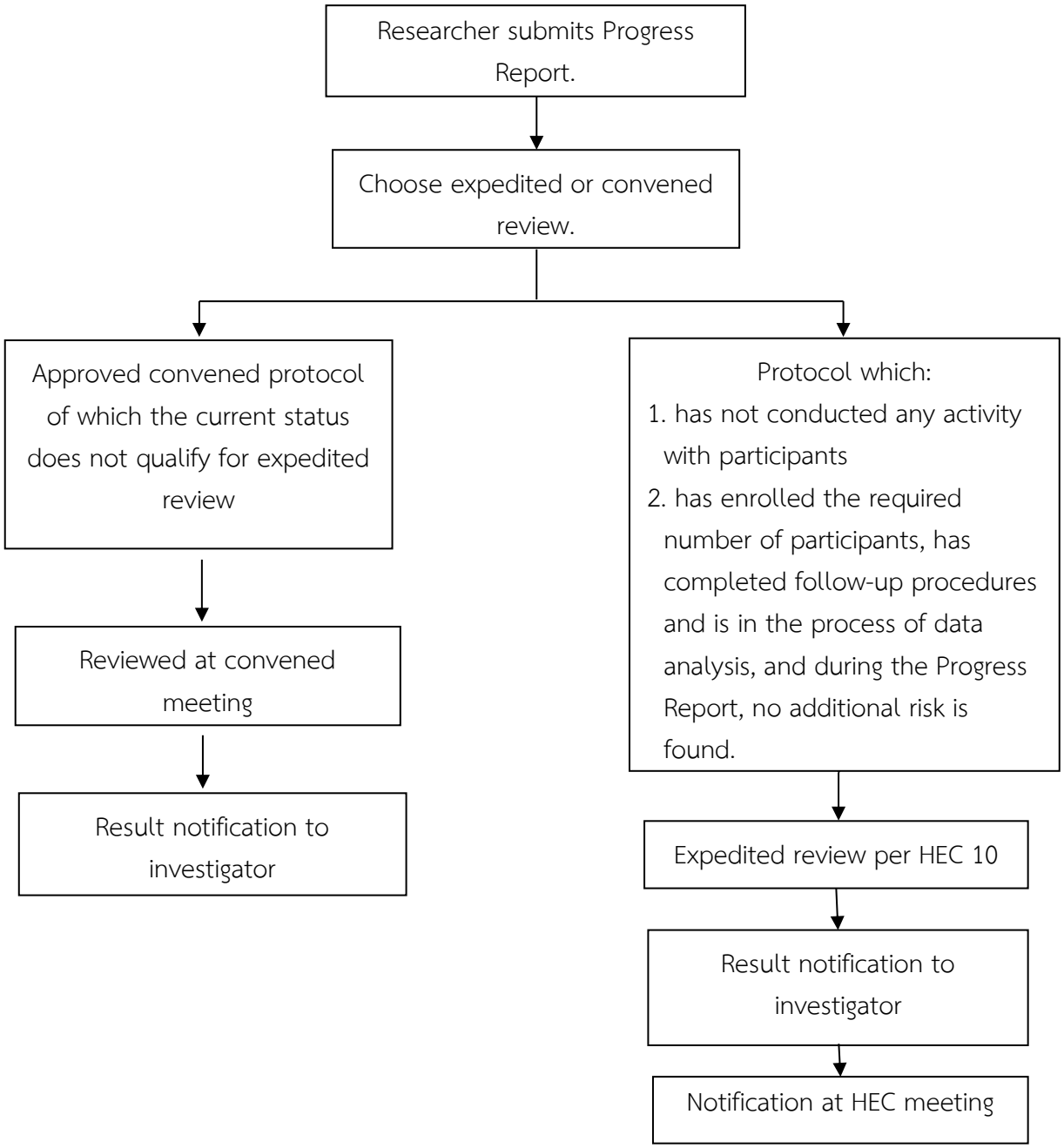
(1) Flow Chart demonstrating HEC Protocol Review Process



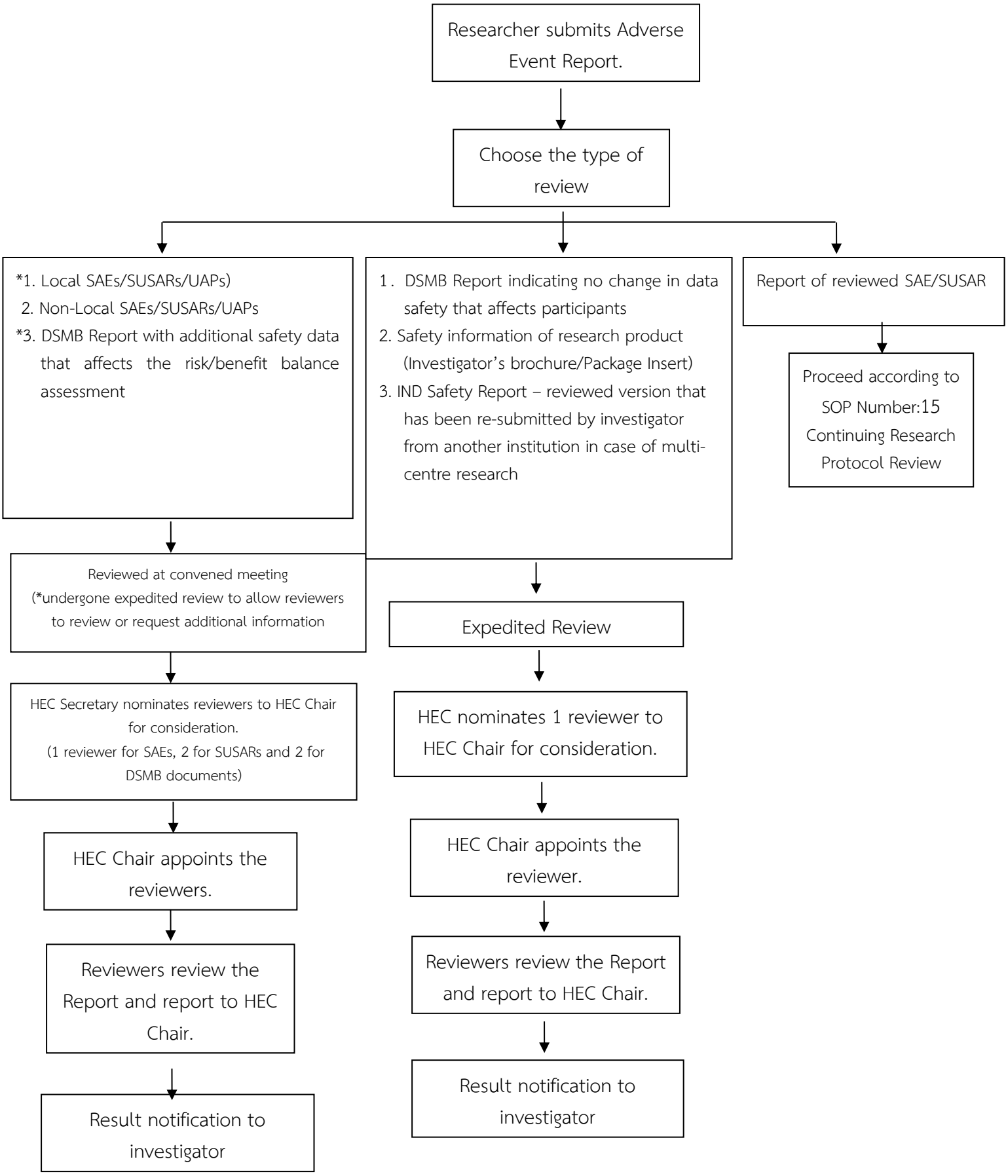
(2) Flow Chart for Amendment Review



(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 participants, the principal investigator shall report the event to the HEC Chair in writing within 24 hours of being informed. In 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 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 participants shall be reported within 15 calendar days after the sponsor has confirmed the SUSAR or after researchers 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 participants, 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 F38.1, item 5 (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 F56.1.
    - The sponsor must report any significant change that increases risk to the participants, 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 F56.1.

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 researchers 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 study 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.

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 close out 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 over extrapolate the findings and use their research in an unethical manner.

Guidance

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

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

7.3 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.

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Glossary

Research

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

Research Involving Human

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 study 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 researchers 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.

Researchers 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 researchers (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 RIHES Director, responsible for considering the initial review, approving the amendment after revision or rejecting, including continuing review to suspend or terminate approval if 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.