Protocol Amendment Decision: IRB's Role

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EDUCATION:

- Internal Medicine and Emergency Medicine Board from Faculty of Medicine Siriraj Hospital, Mahidol University
- Certificate in Bioethics from Asia Collaborative for Medical Education (ACME) Program

PROFESSIONAL EXPERIENCE:

- Associate Professor, Department of Pharmacology, Faculty of Medicine
- Siriraj Hospital, Mahidol University, Bangkok, Thailand
- Assistant dean for research, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
- Vice director of Siriraj Institute of Clinical Research (SICRES)
- Secretary and member of Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University

Protocol Amendment

- A protocol amendment is a change made to an already approved research protocol.
- When a researcher proposes a change to an already approved research protocol, the IRB plays a crucial role in assessing the amendment and deciding whether to approve it.

Protocol Amendment

- The amendment process is crucial for ensuring the ongoing safety and ethical conduct of research studies.
- It allows for necessary adjustments to be made based on new information, unexpected findings, or evolving circumstances.

Key Considerations for IRB Decisions on Protocol Amendments

- Nature of the Change
- Impact on Participants (Participant Safety)
- Scientific Integrity
- Compliance with Regulations
- Transparency and Accountability

Nature of the Change

- **Minor Changes**: These are changes that do not significantly impact the risks, benefits, or scientific merit of the research. The IRB may approve these changes through expedited review.
- Minor modification is defined as a change that entails no more than minimal risk and does not affect an assessment of the benefits and risks of the study, does not change the aims of the study design and is not directly relevant to the determination required for prior approval criteria.

Minor Protocol Amendment

- Administrative changes
- Minor consent form changes
- Minor changes to recruitment procedures, or recruitment materials or submission of new materials to be used in accordance with approved recruitment methods
- Minor changes to study documents such as surveys, questionnaires, or brochures
- New study documents to be distributed to or seen by subjects that are similar in substance to those previously approved

Minor Protocol Amendment

- Changes in payment to subjects or the amount subjects are paid or compensated, that are not significant enough to affect the risk/benefit ratio of the study
- Decrease in the number and volume of sample collections as long as they do not negatively alter the risk/benefit ratio of the study
- Editorial changes that clarify but do not alter the existing meaning of a document
- Addition of or changes in the investigators (Not Principal Investigator)
- Addition of a new study site (in many but not all cases)
- Translations of materials already reviewed and approved by the IRB

Nature of the Change

- **Major Changes**: These are changes that substantially modify the research design, procedures, or risks to participants. The IRB will likely require full review and approval before the changes can be implemented
- The major modification is defined as a change that involves greater than minimal risk, likely increases the risk or discomfort or decreases the benefit, or affects the determination required for prior approval criteria.

Major Protocol Amendment

- Changes that adversely affect the risk/benefit ratio of the study or specifically increase the risk to subjects
- Changes in inclusion/exclusion criteria that impact the risk/benefit ratio of the study
- Significant changes in study design, such as the addition of a new subject population or the elimination of a study aim
- New risk information that is substantial or adversely affects the risk/benefit ratio of the study

Major Protocol Amendment

- Significant changes to the study documents to be distributed or seen by subjects
- New study documents to be distributed or seen by subjects that include information or questions that are substantively different from materials already approved by the IRB.
- New or revised financial conflict of interest management plans

Impact on Participants

- The IRB will assess whether the amendment will increase or decrease the risks to participants.
- They will also consider whether the amendment will affect the informed consent process

Participant Safety

- The primary concern is always the safety and well-being of research participants.
- Any changes that could potentially increase risks or harm to participants must be carefully evaluated and justified.

If the amendment significantly changes the nature or risks of the research, participants may need to be re-consented.

This ensures they have ongoing knowledge and understanding of the study and can make informed decisions.

Scientific Merit

- The IRB will evaluate whether the amendment will improve the scientific validity of the research.
- Amendments should not compromise the scientific validity or integrity of the research.
- Any changes should be well-reasoned and have a clear rationale.
- They will also consider whether the amendment is necessary to achieve the research objectives.

Compliance with Regulations

- The IRB will ensure that the amendment complies with all relevant federal regulations, such as those outlined in the Common Rule.

Transparency and Accountability

- The amendment process should be transparent and accountable.
- All changes should be documented and reviewed by the appropriate ethics committees or regulatory bodies.

Protocol amendment process

- Investigator
  - Identify the Need for an Amendment
  - Prepare the Amendment Document
  - Submit the Amendment for Review
  - Implementation
  - Communication with Participants
- IRB
  - IRB Review: Minor or Major
  - Approval or Rejection

Protocol amendment process

- Investigator
  - Identify the Need for an Amendment
  - Prepare the Amendment Document
  - Submit the Amendment for Review
  - Implementation (After IRB approval)
  - Communication with Participants
- IRB
  - IRB Review: Minor or Major
  - Approval or Rejection: The IRB will either approve the amendment, reject it, or request further modifications.

Amendment Document

- Clearly outline the changes being proposed
- The rationale for the changes
- Any potential impact on participant safety or the study's scientific validity.

The Principal Investigator (PI) is responsible for submitting the requests for changes to the IRB on the Protocol Amendment Form

Protocol Amendment Form

NUSMed Medical Sciences Department Ethics Review Committee (MSDERC)

PROTOCOL AMENDMENT FORM

NUS National University of Singapore

Use this form to request approval for changes to an approved research.
Please send the form and all attachments (with new version numbers & dates) to the DERC (Attn: Ngian Meixing, Cheryl; e-mail: phsnmc@nus.edu.sg).

DERC Reference Code:		Date Approved:	
Principal Investigator:		Supervisor or Corresponding PI:	
Protocol Title *(As stated in your original approval letter)*			

Revision or Amendment Description – check (✓) all that applies:

	Revision to approved protocol	New version no. & date:	
	Revision to approved DERC application form	New version no. & date:	
	Revision to approved Participant Information Sheet & Consent Form (PIS & CF)	New version no. & date:	

1. Describe changes to the approved protocol/DERC application form. Explain in detail the reasons for requesting these changes and which part(s) of the approved document will be amended. Please highlight changes in the revised document.

2. Describe changes to the PIS & CF/recruitment advertisement, etc. Explain which sections of these items are being changed. Please highlight changes in the revised document.

Principal Investigator: [Name and Signature]		Date:	

Protocol Amendment Form

1. Title of Project.....

2. Principal Investigator's name.....

3. Research Site.....

4. Protocol Number .....

5. The amendment effect well-being or may harm to research participants

❒ Yes ❒ No

6. The amendment may need any change in participant information sheet/informed consent form

❒ No

❒ Yes ❒ Consent form Addendum for previously consented subjects, version date.....

❒ New Consent form version date .....

For ❒ New subject

❒ Reconsent for previously consented subjects

7. Please fill in the table below. Please send the amended documents along with this form and modified the related documents (submission form, protocol, etc.), highlight the revised part in form.

Type of Document	Page, Item, Content to be amended	New Content	Reason for Amendment

IRB Process

IRB Secretary with the assistance of the IRB staff
will determine if the revision meets the criteria for minor or major protocol

The protocol change is considered minor and shall be reviewed by the IRB Secretary or the Assigned Amendment Reviewer according to the Expedited Review procedures.

The protocol change is considered major and shall be reviewed by the full board in the next convened IRB meeting.

Full board Review/Major changes

- The IRB Secretary or the Assigned Amendment Reviewer will review the proposed changes
- Make initial suggestions which will be presented to the IRB at the meeting
- The IRB will review and determine whether to approve the amendment, request for more information pending a final decision, or other actions as deemed appropriate.

IRB Assessment Form

TYPE OF AMENDMENT:

[ ] EXPEDITED REVIEW (Check the criteria)

[ ] 1. Administrative changes

[ ] 2. Investigator brochure (No additional risks and not relevant to the subject's willingness to continue participation in trial)

[ ] 3. Minor changes of documents e.g. spelling, protocol format (Editorial changes that clarify but do not alter the existing meaning of a document)

[ ] 4. Minor changes to **recruitment procedures**, recruitment materials or submission of new recruitment materials to be used in accordance with approved recruitment methods.

[ ] 5. **New study documents** to be distributed to or seen by subjects that are similar in substance to those previously approved.

[ ] 6. **Changes in payment** to subjects or the amount subjects are paid or compensated that are not significant enough to coercion/undue influence[

[ ] **FULL BOARD REVIEW** (More than minor changes or that amendment materially affects risks to subjects)

HOW WILL THE AMENDMENT AFFECT THE RISK AND BENEFIT FOR THE SUBJECT?

RISK MAY BE ☐ INCRERASED ☐ THE SAME ☐ DECREASED

POTENTIAL BENEFIT MAY BE ☐ INCRERASED ☐ THE SAME ☐ DECREASED

HOW WILL THE AMENDMENT AFFECT THE PRINCIPLE OF JUSTICE?

☐ FAIR ☐ UNFAIR ☐ NOT APPLICABLE

HOW DOES THE AMENDMENT AFFECT THE INFORMED CONSENT?

[ ] NEW INFORMED CONSENT DOCUMENT IS NOT REQUIRED

[ ] NEW INFORMED CONSENT DOCUMENT IS ADDITION TO THE CURRENT ONE

[ ] NEW INFORMED CONSENT DOCUMENT IS TO REPLACE THE CURRENT ONE

HOW DOES THE AMENDMENT AFFECT TO RE-CONSENT

[ ] RE-CONSENT IS NOT REQUIRED

[ ] RE-CONSENT IS NOT REQUIRED BUT KEEP RESEARCH SUBJECTS INFORMED

IRB Decision Timeline

- The timeline for an IRB decision on a protocol amendment can vary depending on the complexity of the change and the IRB's workload.
- However, most IRBs aim to review and approve minor changes within a few weeks, while major changes may take longer.

The Investigator must obtain IRB approval prior to implementing any changes

The exception to this rule is when changes are necessary to eliminate immediate hazards to subjects

CASE EXERCISE

Old Version

3.หน้า 27 , 16.2 Personal case record

☑ Electronic file

❑ Photos/still photos

❑ Video/moving images

❑ Audio tapes

☑ Others, please specify: Coded identifier of participant on hard copy file

New Version

หน้า 27 , 16.2 Personal case record

☑ Electronic file

☑ Photos/still photos

☑ Video/moving images

☑ Audio tapes

☑ Others, please specify: Coded identifier of participant on hard copy file

CASE EXERCISE

- Minor or Major Amendment
- New Patient Information Sheet (PIS)
- Identifiable data : Patient's face

CASE EXERCISE

Adding Healthy Volunteer

- To validate this method, three healthy volunteer subjects will be recruited for CAR T cell preparation using the same process that will be employed for patients. A total volume of 400 mL of WBC will be collected from each healthy volunteer by leukapheresis.

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CASE EXERCISE

- Minor or Major Amendment
- New Patient Information Sheet (PIS)
- Risk/Benefit

THANK YOU