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### **1. Purpose**

The purpose of this procedure is to describe how protocol amendments are managed and reviewed by the MRIN EC.

### **2. Scope**


This SOP applies to previously approved study protocols but later being amended and submitted for approval to the MRIN EC. Amendments made to protocols may not be implemented until reviewed and approved by the EC.

### **3. Responsibility**

It is the responsibility of the MRIN EC Secretariat to manage protocol amendments. Investigators may amend the contents of protocols from time to time. Protocol amendments may be submitted for either “expedited” review by the Chairperson / Secretariat/members / reviewers or full MRIN EC review. Post approval documents should reviewed by the primary reviewers.

### **4. Flow chart**

<b><u>No.</u></b>	<b><u>Activity</u></b>	<b><u>Responsibility</u></b>
1	Manage the Amendment Package	EC Secretariat
	↓	
2	Notify the Chairperson/Vice Chairperson/Secretary of the MRIN EC	EC Secretariat
	↓	
3	Determine whether Expedited or Full Review	EC Secretary / Vice Chair/Chairperson
	↓	
4	Expedited Review	EC Secretary /Vice Chair/ Chairperson/members
	↓	
5	Full Board Review	EC Secretary / Vice Chair /members / Chairperson
	↓	
6	Amendment Review Process	EC Secretary /Vice Chair/ members / Chairperson
	↓	
7	Notify the Principal Investigator	EC Secretariat
	↓	
8	Store Documents	EC Secretariat

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## **5. Detailed instructions**

### **5.1 Manage the Amendment Package.**

- The amendment package is prepared by the PI.
- Upon receipt of the amendment package, the Secretariat of the MRIN EC should follow the receiving procedure in SOP/007/2020/01.4 (Management of Protocol Submission) and SOP/026/2017/01.2 - Procedure for Maintaining Confidentiality of MRIN EC Documents.
  - Request for Amendment Memorandum** of the Protocol by the Principal Investigator on an existing and previously approved protocol. The memorandum should:
    - State/describe the amendment
    - Provide the reason for the amendment
    - State any untoward effects with original protocol
    - State expected untoward effects because of the amendment
  - Original Amendment Submission Form**
    - Check for completeness and for the presence of the required signatures (Principal Investigator or Medical Advisor of the Institute, if applicable). See ANNEX 1 on page 9.
  - Protocol and Related Documents**
    - The amended version of the protocol and related documents should be provided.
    - The changes or modifications should be underlined or highlighted.

### **5.2 Notify the Chairperson/ Secretary of the MRIN EC.**

- Upon receipt of the amendment package, the Secretariat should inform the Chairperson/Vice Chairperson/Secretary of the MRIN EC verbally or in writing.
- Keep “Sent” and “Received” mail related to the notification of the Chairperson/Vice Chairperson/Secretary in the protocol file under the Correspondence section.
- Send the request for amendment memorandum and the protocol and related documents to the Chairperson/ Vice Chairperson/Secretary within 5 working days of receipt by the Secretariat.
- Follow MRIN EC SOP/026/2017/01.2 in preparing and distributing the documents.
- After review of the materials, the Chairperson/Vice Chairperson/Secretary will determine whether the protocol requires expedited or full review.

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### 5.3 Determine whether exempted, expedited or full review.


- Refer to SOP/009/2020/01.4 for Expedited / Exempted Review.
- Refer to SOP/010/2020/01.4 for Full Review.
- Protocol amendment which increases risk to study participants, as judged by the Chairperson/Vice Chairperson/Secretary, such as a change in study design, which may include but is not limited to:
  - additional treatments or the deletion of treatments
  - any changes in inclusion/exclusion criteria
  - change in method of dosage formulation, such as, oral changed to intravenous
  - significant change in the number of subjects (Increase: if there are <20 subjects enrolled, change of 5 is significant; if there are >20 subjects enrolled, a change of 20% is significant – Decrease: if the decrease in the number of subjects alters the fundamental characteristics of the study, it is significant)
  - significant decrease or increase in dosage amount
- If the Chairperson/Vice Chairperson/Secretary decides the protocol requires full board MRIN EC approval, the Chairperson/Vice Chairperson/Secretary will indicate this decision on the Checklist, sign and date the form.
- The Secretariat places the protocol amendment request on the agenda for the next convened meeting.
- The following documents are distributed to each MRIN EC member:
  - the amendment's revision documents to clearly identify each change.
  - requested changes to the consent form, if applicable
- If an amendment is received just prior to the MRIN EC meeting, the Chairperson/Vice Chairperson/Secretary may decide to review the amendment in full MRIN EC, even though the amendment may be expedited.

### 5.4 Expedited/Exempted Review

- Refer to SOP/009/2020/01.4 for expedited/exempted review procedure.

### 5.5 Full Review by the MRIN EC


- Refer to SOP/010/2020/01.4 for full Board Review.
- See section 5.6

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## 5.6 Protocol Amendment Review Process

### 5.6.1 Review amended protocols

- Use the process outlined in the Application Assessment Form (see MRIN EC SOP/008/2020/01.5 and SOP 010/2020/01.4) to review amended protocols and protocol-related documents.
- Note recommendations for changes to the protocol and/or informed consent requested by MRIN EC Members in the minutes as “with modifications made by MRIN’ and will be communicated to the clinical trial office???” or investigator.
- The Chairperson/Vice Chairperson/Secretary or designee calls for a consensus / vote on the proposed amendment to:
  - Approve the protocol amendment as is with no modification of the informed consent
  - Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with follow-up by the Chairperson/ Vice Chair person/Secretary
  - Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with follow-up by the Chairperson/ Vice Chairperson/Secretary
  - Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with a follow-up full MRIN EC review
  - Suspend the study, until further information is obtained
  - Not suspend the study as currently approved, but request further information regarding the amendment and the effects of the amendments on the approved study
  - Not approved the amendment request, stating the reason – but allow the study to continue as previously approved
- If the MRIN EC approves the protocol amendment, the Secretariat staff communicates this decision to the investigator.
- If the MRIN EC does not approve the protocol amendment, the Chairperson/ Vice Chairperson/Secretary notify the investigator in writing of the decision and the reason for not approving the amendment.
- If the MRIN EC votes to require modifications to any of the documents, or the protocol amendment, the Secretariat sends a written request about the specific changes to the investigator asking him or her to make the necessary changes and resubmit the documents to MRIN Ethics Committee.

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- The Chairperson/Vice Chairperson/Secretary complete a decision form (AF/01-013/2020/01.6) after the MRIN EC has reached its decision.
- Keep the forms, minutes of the meeting relevant to the discussion and the decision reached by the MRIN EC as the official records of the amendment review process.

### **5.6.2 Communication of the Decision**

The Chairperson/Vice Chairperson/Secretary **could communicate to** the Principal Investigator after the MRIN EC meeting in writing as soon as possible, but no later than 7 working days following the review.

### **5.6.3 Completion of the Amendment Submission Form**

- The Chairperson/Vice Chairperson/Secretary must sign and date the original version of this form and return this to the Secretariat no later than 7 working days after the review.
- Addition of Amendment to the Protocol Number  
The Secretariat assigns a letter to the protocol number that corresponds to the number of the amendment. For example:  
The third amendment to MRIN. 015/01-03 would be formatted as: MRIN. 015/01-03Cn (n refers to number of amendment submission)
- Record the amended protocol number on the form.
- The Secretariat signs and dates the original version of the form.

### **5.7 Notify the Principal Investigator.**


- Send a signed and dated notification of decision to the Principal Investigator (P.I.) for their records no later than 7 working days.

### **5.8 Store documents.**

- Place the original completed documents, the “clean” version (delete) of the protocol and related documents in the protocol file with the other documents pertaining to the amendment.

## **6. Glossary**

**Amendment protocol package**      A package of the amended parts and related documents of the protocol, previously approved by the MRIN EC. In the course of the study, the PI may decide to make changes in the protocol.

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**Clinical trial office**      An institute or an office where the study takes place and where the principal investigator and/or his/her staff may be reached.


**Expedited approval**      An MRIN EC approval granted only by the Chairperson of the .MRIN EC or a designated MRIN EC member (not the full MRIN EC) for minor changes to current MRIN EC approved research activities and for research which involves no more than minimal risk, as stated in the SOP/009/2020/01.4.

## **7. Annex**

Annex 1      AF/01-013/2020/01.6 Protocol Amendment Submission Form  
Annex 2      AF/02-013/2020/01.6 Document History

## **8. References**

- Peraturan Pemerintah Republik Indonesia Nomor 39 Tahun 1995 tentang Penelitian dan Pengembangan Kesehatan, [http://www.litbang.depkes.go.id/unduh\\_pp](http://www.litbang.depkes.go.id/unduh_pp).
- Code of Federal Regulation (CFR), 21 456.110, The United States of America, 1998.
- Operational Guidelines for Ethics Committees that Review Biomedical Research, World Health Organization, 2000, Geneva.
- Surveying and Evaluating Ethical Review Practices, World Health Organization, 2002, Geneva.
- International Conference on Harmonisation (ICH) Harmonised Tripartite : Guideline for Good Clinical Practice E6(R1), Current Step 4 version dated 10 June 1996, November 2005, November 2016
- Undang-undang Kesehatan No. 36 Tahun 2009 pasal 44.
- Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants, 2011, World Health Organization, [www.who.int](http://www.who.int).
- Pedoman Nasional Etik Penelitian Kesehatan, Komisi Nasional Etik Penelitian Kesehatan, 2011.
- SIDCER Self-Assessment Tool, <http://www.fercap-sidcer.org/selftool.php>, accessed January 2013.
- Relevant SOPs SOP/007/2020/01.4, SOP/008/2020/01.5, SOP/009/2020/01.4, SOP/010/2020/01.4 and SOP/026/2017/01.2


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**Annex 1**  
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**Protocol Amendment Submission Form**


PROTOCOL NUMBER:		SUBMITTED DATE:	
PROTOCOL TITLE:			
PRINCIPAL INVESTIGATOR:			
INSTITUTE:		Telephone:	
PARENT PROTOCOL APPROVED PERIOD DATE:		NO. OF AMENDMENT:	
A. Summary of previous protocol amendment (if any)			
Approval amendment nomor.	Original Protocol	Short description of the amendment	Approved Date
B. Describe of amendment requested			
C. Reason of amendment requested			
D. State any untoward effects with original protocol ? maksudnya apa			
E. State expected untoward effects because of the amendment ? perbedaannya apa dengan E			
SIGNATURES:			
_____ Principal Investigator			Date:.....



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TYPE OF AMENDMENT REQUESTED: filled by Secretary/Vice Chairperson/Chairperson <input type="checkbox"/> EXPEDITED <input type="checkbox"/> EXEMPTED <input type="checkbox"/> FULL BOARD											
COMMENTS: (filled by Reviewer) : ..... ..... .....											
SIGNATURES:  _____ Date:..... Protocol Reviewer											
<table border="1" style="width: 100%;"> <tr> <td colspan="2">DECISION :</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Approved</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Minor revision</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Major revision</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Disapproved</td> </tr> </table>		DECISION :		<input type="checkbox"/>	Approved	<input type="checkbox"/>	Minor revision	<input type="checkbox"/>	Major revision	<input type="checkbox"/>	Disapproved
DECISION :											
<input type="checkbox"/>	Approved										
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APPROVALS  _____ Date: ..... Chairperson/Vice Chairperson, MRIN EC  COMPLETION  _____ Date: ..... Secretary, MRIN EC											

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Annex 2  
Form AF/02-013/2020/01.6

Document History

Author	Version	Date	Description
EC Members	01.0	2 January 2013	<b>Final version</b>
Ivet, Lia, Mona	01.1	11 October 2014	<ol style="list-style-type: none"> <li>1. Synchronize the topic number and SOP number</li> <li>2. Format Document History : Author, Version, Date and Description of the main change</li> <li>3. Post approval documents should be reviewed by the primary reviewers in SOP 13 (Section 5.6.1)</li> <li>4. Form Annex 1 : addition of section for reviewer comments and EC decision</li> </ol>
Ivet, Lia, Mona	01.2	15 November 2014	<ol style="list-style-type: none"> <li>1. “Post approval documents should be reviewed by primary reviewers” put under Section 3</li> </ol>
Lia, Mona	01.3	20 February 2016	<ol style="list-style-type: none"> <li>1. Annex 1: Replace Decision Approved with Minor revision to be Minor Revision and Replace Approved with Major Revision to be Major Revision</li> </ol>
Irawan Yusuf, Budhianto Suhadi	01.4	1 April 2017	<ol style="list-style-type: none"> <li>1. Delete Komisi Etik Penelitian Kesehatan (KEPK) on the header</li> <li>2. Item 5.3. Box 4 to add the word” board”</li> <li>3. Item 5.6.2 : add the sentence “Refer to SOP no.010/2014.01.2 for communication of the decision to PI”</li> </ol>
LSH, MW, IS	01.5	2 January 2019	<ol style="list-style-type: none"> <li>1. Item 4 : to add Vice Chairperson</li> <li>2. Item 4.7 : delete Secretary</li> <li>3. Item 5.2 Box 1 -6 : to add Vice Chairperson</li> <li>4. Item 5.3 Box 3,4 &amp; 7 ; to add Vice Chairperson</li> <li>5. Item 5.6.1. : Box 3 &amp; 7 to add VP; Box 4 :delete Secretary</li> <li>6. Item 5.6.2. : to add Vice Chairperson</li> <li>7. Item 5.6.3 : to dd Vice Chairperson</li> <li>8. Item 5.6.3 : Replace time line from 5</li> </ol>

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			working days to 7 working days 9. Annex 1 : to add section list of amendment to be filled up by PI & amendment of requested : to add Vice Chairperson and chairperson 10. Annex 2 : to add Vice Chairperson on the approval
LSH,MW,DS R	01.6	02 January 2020	1. 5.3 : title include exempted 2. 5.6,.1 box 2 : add statement of “and SOP 010/2020/01.4” 3. 5.6.1,box 2 : clinical trial office??? 4. 5.6.1,box 3 : add “ consensus” 5. 5.6.2 : Delete the statement “ Refer to SOP no.010/2020/01.4 for communication of the decision to PI” 6. 5.6.3 : To add numbering of amendment, for example 015/01-03Cn (n refers to number of amendment submission) 7. 5.7, box 1 : replace “Amendment Submission Form” with “ Notification of Decision” 8. 5.7 box 2 : Delete 9. 5.8 : delete “ the “clean” version of the protocol 10. 7. References : <ul style="list-style-type: none"> <li>• Delete link WHO</li> <li>• Delete FERCAP SOP</li> <li>• Add ICH Nov 2016</li> </ul>