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1. Purpose

This procedure describes how continuing reviews of previously approved protocols are managed by the MRIN EC.

The purpose of the continuing review is to monitor the progress of the entire study, not just the changes in it, to ensure continuous protection of the rights and welfare of research participants. Continuing review of the study may not be conducted through an expedited review procedure, unless 1) the study was eligible for, and initially reviewed by, an expedited review procedure; or 2) the study has changed such that the only activities remaining are eligible for expedited review.

2. Scope

This SOP applies to conducting any continuing review of study protocols involving human subjects at intervals appropriate to the degree of risk but not less than once a year. Depending upon the degree of risk to the participants, the nature of the studies, and the vulnerability of the study participants and duration of the study, the MRIN EC may choose to review or monitor the protocols more frequently.

3. Responsibility

It is the responsibility of the MRIN EC Secretariat to remind the MRIN EC and the principal investigators regarding study protocols that should be continuously reviewed; Progress report must be submitted when 50% of data have been collected or at the mid poin of the study period, which ever the earliest. The Chairperson/ Secretary is responsible for determining the date of continuing review. Progress Report is reviewed by the primary reviewers.

The MRIN EC is responsible for reviewing the progress made in the protocol, the occurrence of unexpected events or problems, and the rate of accrual of participants. The protocol informed consent documents and assent documents are examined to ensure that the information remains accurate.

The MRIN EC has the same options for decision making on a continuing review package as for an initial review package. The decision is made as approved, minor revision, major revision, disapproved.

4. Flow chart

No.	Activity	Responsibility
1	Determine the date of continuing review	EC Secretary and Chairperson/Vice Chairperson
	↓	
2	Notify the study team	EC Secretariat
	↓	
3	Manage continuing review package upon receipt	EC Secretariat
	↓	
4	Notify the members of the MRIN EC/KEPK MRIN	EC Secretariat
	↓	
5	Prepare meeting agenda	EC Secretariat and Secretary
	↓	
6	Protocol review process	EC Secretary, Members and Chairperson/Vice Chairperson
	↓	
7	Store original documents	EC Secretariat

5. Detailed instructions

5.1 Determine the date of continuing review.

- ☐ Look through the document archives for the due date of continuing reviews.
- ☐ Plan for continuing review meeting at least 30 days ahead
- ☐ Consult the Chairperson/ Vice Chairperson/Secretary for scheduling the Board meeting date.

5.2 Notify the principal investigator or the study team

- ☐ Inform the Study Team at least **one months in advance** of the due date for the continuing review by e-mail or other appropriate means.
- ☐ Notify to the study team to use Continuing Review Application Form (AF/01-014/2020/01.6) to fill up.
- ☐ Keep the informed notice in the correspondence file.
- ☐ Allow the Study Team sufficient time to collate the information and to prepare a report package required for the continuing review.

5.3 Manage continuing review package upon receipt.

- ☐ Receive a package of continuing review for each protocol prepared and submitted by the Study Team.
- ☐ Upon receipt of the package, the Secretariat of the MRIN EC should perform the following:

5.3.1 Initial and date the submission package

- ☐ See SOP/007/2020/01.4 for procedures on receipt of submitted packages.

5.3.2 Verify the contents of the package.

- ☐ Make sure that the contents of the package include:
  - ☐ **Continuing Review Application Form**
    - ❑ Check for complete information and for the presence of the required signatures.
    - ❑ See ANNEX 1 for the Continuing Review Application Form (AF/01-014/2020/01.6).
  - ☐ **Continuing Review Memorandum** with progress report
    - ❑ Summarize the progress of the protocol since the time of the last review.
    - ❑ Include information about the number of participants enrolled to date and since the time of the last review, an explanation for any "yes" answers on the application form and a discussion of scientific development, either through the conduct of this study or similar research that may alter risks to research participants.
  - ☐ **Current Informed Consent Document**

- ☐ Verify electronic Informed Consent Document (where applicable).
  - ☐ Check if the electronic copy for matches the hard copy submitted by the study team.
  - ☐ Store the hard copy with the submitted documents.
  - ☐ Clearly identify the document as the hard copy of the electronic informed consent document.
  - ☐ Ensure that the version of the informed consent document is the most recently approved informed consent document.

5.3.3 Disseminate review package.

- ☐ Send email to both members and reviewers, the original continuing review package in accordance with MRIN EC SOP/

Procedures for Maintaining Confidentiality of MRIN EC Documents.

5.3.4 Store the continuing review package.

- ☐ Store the original package in the protocol specific file.

5.4 Notify the Members of the MRIN EC.

- ☐ Distribute the protocol progress report and the current informed consent document to the MRIN EC.

5.5 Prepare meeting agenda.

- ☐ See SOP/021/2020/01.6 for procedures on the preparation of meeting agenda.
- ☐ Place the review on the agenda for the meeting of the MRIN EC
- ☐ Distribute the materials to the MRIN EC members by electronic mail (e-mail) according to SOP/026/2017/01.2 (Procedures for Maintaining Confidentiality of MRIN EC Documents) at least one and a half to two weeks in advance of the scheduled meeting.
- ☐ Keep copies of "sent" e-mail in the Correspondence Section of the protocol specific file.
- ☐ Record and keep the MRIN EC members' response upon receipt of the agenda in the member correspondence file.

5.6 Protocol Review Process

5.6.1 Continuing Review Application Form

- ☐ Use the Continuing Review Application Form (AF/01-014/2020/01.6) to guide the review and deliberation process.
- ☐ Sign and date the Continuing Review Application Form by the Chairperson/Vice Chairperson/Secretary of the MRIN EC after a decision has been reached.
  - ☐ The completed Continuing Review Applications Form is the official record of the decision reached by the MRIN EC for the protocol.
  - ☐ Maintain and keep the form and minutes of the meeting relevant to the continuing review as part of the official record of the review process.

5.6.2 Preliminary Communication of the Decision

- ☐ Preliminary Written Communication of the Decision
  - ☐ The Chairperson/Vice Chairperson/Secretary must send an electronic version of the completed Continuing Review

Application Form to the Secretariat no later than 7 working days after the review has taken place.

- ☐ The Secretariat, in turn, forwards the result to the study team (by e-mail). "Sent" or "Received" e-mails are filed in the protocol file under "Correspondence".

5.6.3 Final Documentation and Communication of the Decision

- ☐ Complete the printed version of the Continuing Review Application/ Assessment Form by the Chairperson/Vice Chairperson/Secretary of the MRIN EC:
  - ☐ Sign and date the printed version of the form containing the decision and return this to the Secretariat.
  - ☐ Complete the process within 7 working days of the MRIN EC meeting.
- ☐ Complete the original version of the Continuing Review Application Form by the Chairperson/Vice Chairperson/Secretary:
  - ☐ Sign and date the original version of the form.
  - ☐ The Secretariat must sign and date the form.

5.7 Store original documents.

- ☐ Place the original completed documents with the other documents in the Continuing Review Package in the protocol file.

6. Glossary

Approved Protocols	Protocols that have been *approved* by the MRIN EC may proceed. Protocols that have been *approved with recommendations* by the MRIN EC may not proceed until the conditions set by the MRIN EC in the decision have been met. Protocols should be amended and submitted to the MRIN EC within *one* month for re-review.

7. Annex

Annex 1	AF/01-014/2020/01.6	Continuing Review Application Form (2 pages)
Annex 2	AF/02-014/2020/01.6	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
- 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,
- 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.
- Associated SOP/007/2020/01.4, SOP/021/2020/01.5 and SOP/026/2017/01.2.
- Standard Operating Procedures UP Manila,2019

Annex 1
Form AF/01-014/2020/01.6
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Continuing Review Application Form

PROTOCOL No.:

PROTOCOL TITLE:

Ethical Approval period :

INSTITUTE MEDICAL ADVISOR:

ACTION REQUESTED:
- ❑ Renew - New participant accrual to continue
- ❑ Renew - Enrolled participant follow up only
- ❑ Terminate - Protocol discontinued

HAVE THERE BEEN ANY AMENDMENTS SINCE THE LAST REVIEW?
- ❑ NO
- ❑ YES (Describe briefly in attached narrative)

SUMMARY OF PROTOCOL PARTICIPANTS:
- _____ Accrual ceiling set by MRIN EC/KEPK MRIN
- _____ New participants accrued since last review
- _____ Total participants accrued since protocol began

ACCRUAL EXCLUSIONS
- ❑ NONE
- ❑ MALE
- ❑ FEMALE
- ❑ OTHER (specify: _____)

IMPAIRED PARTICIPANTS
- ❑ None
- ❑ Physically
- ❑ Cognitively
- ❑ Both

HAVE THERE BEEN ANY CHANGES IN THE PARTICIPANT POPULATION, RECRUITMENT OR SELECTION CRITERIA SINCE THE LAST REVIEW?

- ❑ NO
- ❑ YES (Explain changes in attached narrative)

HAVE THERE BEEN ANY CHANGES IN THE INFORMED CONSENT PROCESS OR DOCUMENTATION SINCE THE LAST REVIEW?

- ❑ NO
- ❑ YES (Explain changes in attached narrative), please attach current informed consent document…..

HAS ANY INFORMATION APPEARED IN THE LITERATURE, OR EVOLVED FROM THIS OR SIMILAR RESEARCH THAT MIGHT AFFECT THE MRIN EC/KEPK MRIN'S EVALUATION OF THE RISK/BENEFIT ANALYSIS OF HUMAN SUBJECTS INVOLVED IN THIS PROTOCOL?

- ❑ NO
- ❑ YES (Discuss in the attached narrative)

HAVE ANY UNEXPECTED COMPLICATIONS OR SIDE EFFECTS BEEN NOTED SINCE LAST REVIEW?
- ❑ NO
- ❑ YES (Discuss in the attached narrative)

HAVE ANY PARTICIPANTS WITHDRAWN FROM THIS STUDY SINCE THE LAST MRIN EC/KEPK MRIN APPROVAL?
- ❑ NO
- ❑ YES (Discuss in the attached narrative)

INVESTIGATIONAL NEW DRUG/DEVICE
☐ NONE ☐ IND ☐ IDE
FDA No. ……..
Name: ……
Sponsor: ……
Holder: ……

IONIZING RADIATION USE (X-rays, radioisotopes, etc)
- ❑ None
- ❑ Medically indicated only

HAVE ANY PARTICIPATING INVESTIGATORS BEEN ADDED OR DELETED SINCE LAST REVIEW?
- ❑ NO
- ❑ YES (Identify all changes in the attached narrative)

HAVE ANY NEW COLLABORATING SITES (INSTITUTIONS) BEEN ADDED OR DELETED SINCE THE LAST REVIEW?
- ❑ NO
- ❑ YES (Identify all changes and provide an explanation of changes in the attached narrative)

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CHANGE IN MEDICAL ADVISOR / INVESTIGATOR? ❑ NONE ❑ DELETE:…… ❑ ADD: ……	HAVE ANY INVESTIGATORS DEVELOPED AN EQUITY OR CONSULTATIVE RELATIONSHIP WITH A SOURCE RELATED TO THIS PROTOCOL WHICH MIGHT BE CONSIDERED A CONFLICT OF INTEREST? ❑ NO ❑ YES (Append a statement of disclosure)

Results:	**Include the information below on the progress report** (Use extra blank paper, if more space is required.) 1. Have there been any changes to the project since the previous ethics approval (Renewal or Amendment)? 2. Please list any Amendments that have been submitted since the date indicated on the Letter of Initial Ethics Approval 3. Please provide a brief summary of the progress of the study. 4. If there is any protocol deviation / violation, give a brief explanation. 5. Include information surrounding study implementation details (such as the recruitment of participants) and whether or not the study is progressing as planned. 6. Please document any issues that might pose a challenge to the study meeting its proposed timelines. Attach supporting documents if necessary. 7. During the course of the project have any ethical concerns or difficulties arisen? 8. Has your study experienced any unanticipated

	problems? 9. Have all SAEs been reported since your study was initially approved? 10. If SAEs have occurred but have not been reported, please explain why they have not been reported, give details of these events, and provide your opinion on whether these are study-related, whether they affect the ethics of continuing the study, and whether they necessitate any changes to the informed consent process. Please provide an overall assessment.
Signature of P.I.:	Date:

Annex 1
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Please mark and fill comments if any suggestion or recommendation from the reviewers.

Assessment by the Primary Reviewer	
Do the risks to the study participants remain reasonable in relation to anticipated benefits ☐ Yes ☐ No	Comments :
Are there new findings in the Investigator Brochure or literature (e.g important toxicity or adverse event information) that need to be included in the informed consent ☐ Yes ☐ No	Comments :
Is there need to revise the ICF ☐ Yes ☐ No	Comments :
Is there need to reconsent subjects enrolled in the study ☐ Yes ☐ No	Comments :
Are there concerns about conduct of the research team (e.g suspension of medical license, frequent protocol violation, patient or third party complaints, etc) or institutional commitment that may affect patients safety? ☐ Yes ☐ No	Comments :
Are there concerns about patient safety, inability to comply with the protocol, high dropout rate that affect study implementation ☐ Yes ☐ No	Comments :

MRIN EC Decision:	☐ Approved ☐ Minor revision ☐ Major revision ☐ Disapproved

SIGNATURES:

_____ Date:……

Protocol Reviewer

APPROVALS

_____ Date:……

Chairperson/Vice Chairperson, MRIN EC

COMPLETION

_____ Date:……

Secretary, MRIN EC

Annex 2
Form AF/02-014/2020/01.6

Document History

Author	Version	Date	Description
EC Members	01.0	2 January 2013	**Final version**
Ivet, Lia, Mona	01.1	11 October 2014	1. Synchronize the topic number and SOP number 2. Format Document History : Author, Version, Date and Description of the main change 3. Section 3 : a. Progress report must be submitted when 50% of data have been collected b. The decision is made as approved; approved with minor revision; approved with major revision, pending, or disapproved. 4. Section 5.1. : Timeline should be changed from 60 days to 30 days 5. Section 5.6.1. Post approval documents should be reviewed by the primary reviewer 6. Annex 1 : Signature MRIN/Medical Advisor and MRIN Director should be corrected & EC Decision
Ivet, Lia, Mona	01.2	15 November 2014	1. Section 5.6.1 :"Post Approval Documents" replace with "Progress Report" 2. "Progress Report is reviewed by primary reviewer" put under Sec 3
Lia, Mona	01.3	20 February 2016	1. Annex 1: Replace Decision Approved with Minor revision to be Minor Revision and Replace Approved with Major Revision to be Major Revision
Suryani As'ad, Ivet Suriapranata	01.4	1 April 2017	1. Delete Komisi Etik Penelitian Kesehatan (KEPK) on the header 2. Item 3, paragraph 3: Revise sentence "The decision is made as approved; approved with minor revision; approved with major revision,

			pending, or disapproved" to "The decision is made as approved, major revision, minor revision and disapproved" 3. Delete Item 5.8. Revise Flow Chart accordingly. 4. Annex 1: Add "Ethical Approval Period" as a new line. 5. Annex : Add the sentence "Refer to Guideline for PI item 5 (Procedure for Continuing Review) in the Results part
MRIN EC Members	01.5	2 January 2019	1. Item No. 4.1 & 4.6. : to add Vice Chairperson 2. Item 5.1 : to add Vice Chairperson 3. Item 5.6.1 Box 2 : to add Vice Chairperson 4. Item 5.6.2. Box 1 & box 2 : to add Vice Chairperson 5. Annex 1 : to include Vice Chairperson on approval and add information procedure for continuing review from the guideline
MW,IS,LSH, GE	01.6	2 January 2020	1. SCOPE : Delete the word of "And Animal" 2. 5.1, box 2 : delete the sentence of " and as close possible to the due date or the anniversary…..of the protocol" 3. 5.2, box 2 : change email with notify 4. Annex : Add statement were the protocol deviation/report summarize... taken and Assesment by Primary Reviewers 5. Annex : add information to attach : current informed consent document and delete the word of " submssion date" 6. 5.4 : add the word of "current" 7. 5.5. Box 2 delete statement which....effective date 8. 5.6..2 Box 2 : replace continuing...form with the result

			9. References : • Delete link WHO • Delete FERCAP SOP • Add ICH Nov 2016