# CONDUCTING SITE VISITS

Cecilia A. Jimeno, MD

UPM REB Panel 1 Chair

# References


- ICH GCP (E6)
- National Ethical Guidelines for Research Involving Human Participants 2022 (Philippines)
- SOPs of UPM REB (University of the Philippines Manila REB)

# Outline of Discussion

- What is a site visit by an REC?
- Reasons for RECs to do site visits & criteria for selection of sites
- Procedures involved in the site visit: composition, preparation, conduct, reporting

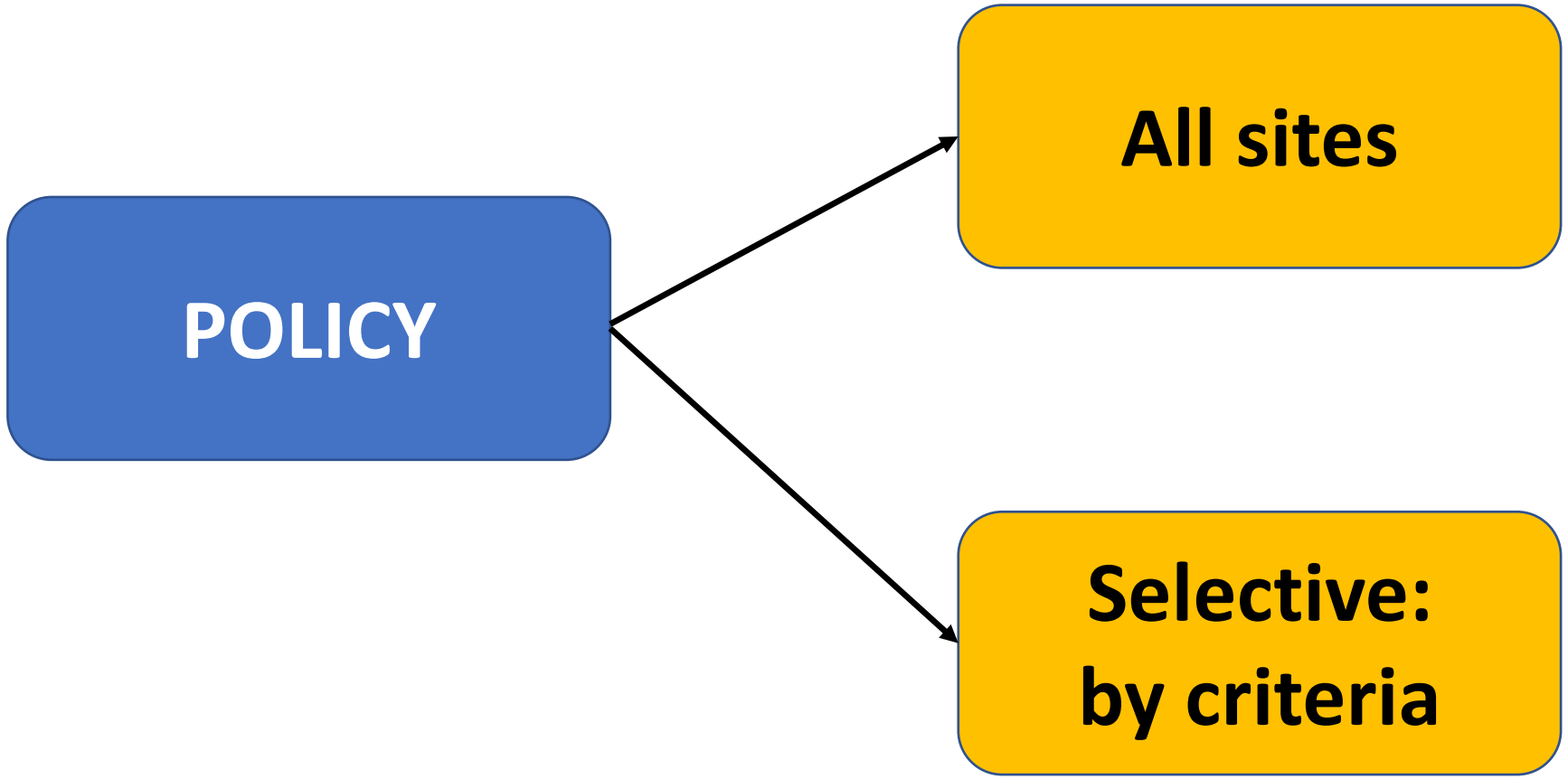
# What is a site visit by an REC?

- Part of post-approval activities of the REC for protocols that it has approved.
- Form of **audit** done by representatives of the ethics committee to assess:
  - Compliance with REC-approved protocol & related documents
  - Determine consistency of IRB file with site file inventory
  - Verify specific issues e.g. reports of high volume of protocol deviations, complaints from participants, or critical events.

# ICH-GCP (E6): Responsibilities of IERB/IERC

"3.1.4 The IRB/IEC should conduct **continuing review** of each ongoing trial at intervals appropriate to the degree of risk to human subjects, but at least once per year."

# Selection of Study Sites to Visit



# Reasons for RECs to do Site Visits (NEGRIHP 2022)

1. Significant number of serious adverse events,
2. New study sites,
3. Significant number of non- compliance reports submitted or the nature of the deviation is grave,
4. Suspicious conduct,
5. Failure to submit required reports.

# Criteria for Selection of Sites to be Visited

1. The nature of the study being conducted (i.e. high risk studies).
2. Frequent non-submission or failure to submit continuing review requirements,
3. Reports of major protocol noncompliance [or large number of reports],
4. Significant number of serious adverse events,
5. Reports of complaints from study participants,
6. Or for other reasons upon recommendation of the Panel.

# Criteria for Selection of Sites to be Visited-2

- Study sites may also be selected for Site Visit upon recommendation of various committees such as Serious Adverse Event and Report of Pregnancy Committee, or by the SJREB for participating sites.
- The decision for Site Visit is deliberated on during a full board meeting of the UPMREB Panel that issued the ethical clearance or approval to a study.

# SOP’s on Site Visit by the REC

**Objective**: Compliance with REC-approved protocol and related documents, determination of consistency of REC files with site file inventory

**Scope**: Persons, offices, documents OR processes covered by SOP

**Responsibilitie**s of typical personnel involved, e.g. Site Visit Team, Staff which handles all administrative processing to organize the visit, the Chair, composition of the site visit team

# Composition of the site visit Team

- Members of this team are assigned by the Panel Chair.
- At **least** three (3) people:
  - Primary reviewers of the protocol (at least one),
  - SAE Committee member (at least one),
  - One (1) Panel Member.
  - REC Staff (optional)
- The Site Visit Team members are informed of their assignment through the issuance of a Notice of Site Visit.

# **How are site visits done?** NEGRIHP 2022

1. **Prior agreement of schedule**: REC shall inform the researchers of the visit at a date agreeable to both.
2. **What are reviewed?** The informed consent to see if an updated version is being used, examine study files, observe the informed consent process; if possible, inspect the study site, and interview participants.
3. **Feedback:** After the site visit, a report is given to the principal researcher and the REC.
4. **Actions:** The REC may recommend corrective & preventive actions for observations made.

# Notification of PI of Date of site visit

- The Panel Chair, through the Secretariat, informs the PI at **least 2 weeks** before the scheduled visit through a letter.
- A copy of the Site Visit Report form is attached to the letter (to make the site aware of how the visit will be done & evaluation points)
- The letter provides site visit schedule details & instructions on what the PI needs to prepare such as documents and files that will be used for the Site Visit, as well as orderly preparation of the site.

# What is Evaluated during the site visit?

Documents

Processes

Infrastructure in relation to ensuring privacy, confidentiality & security of documents (patient information).

# Procedure 1: Review of Documents

- Study Protocol – is site using the most recently approved version?
- Informed consent documents –recent version?
- Include compensation logs, advertisements, etc
- Post-approval documents: amendments, continuing review, SAE/SUSAR reports (have these been reported or acted on).
- **Site delegation log.**

# Procedure 2: Interview

- Principal Investigator and/or Co-investigator
  - Overview of Clinical Trial site management
  - Description of the Informed Consent Process (recruitment, verification of the identity of study participants)
- Staff/Research Assistant/Study Coordinator
  - Role in the Clinical Trial site management/operations
  - Description of the Informed Consent Process
  - Description of file management, including procedures for accessing protocol related files.
- ?? Study Participants

# Procedure 3: Observation

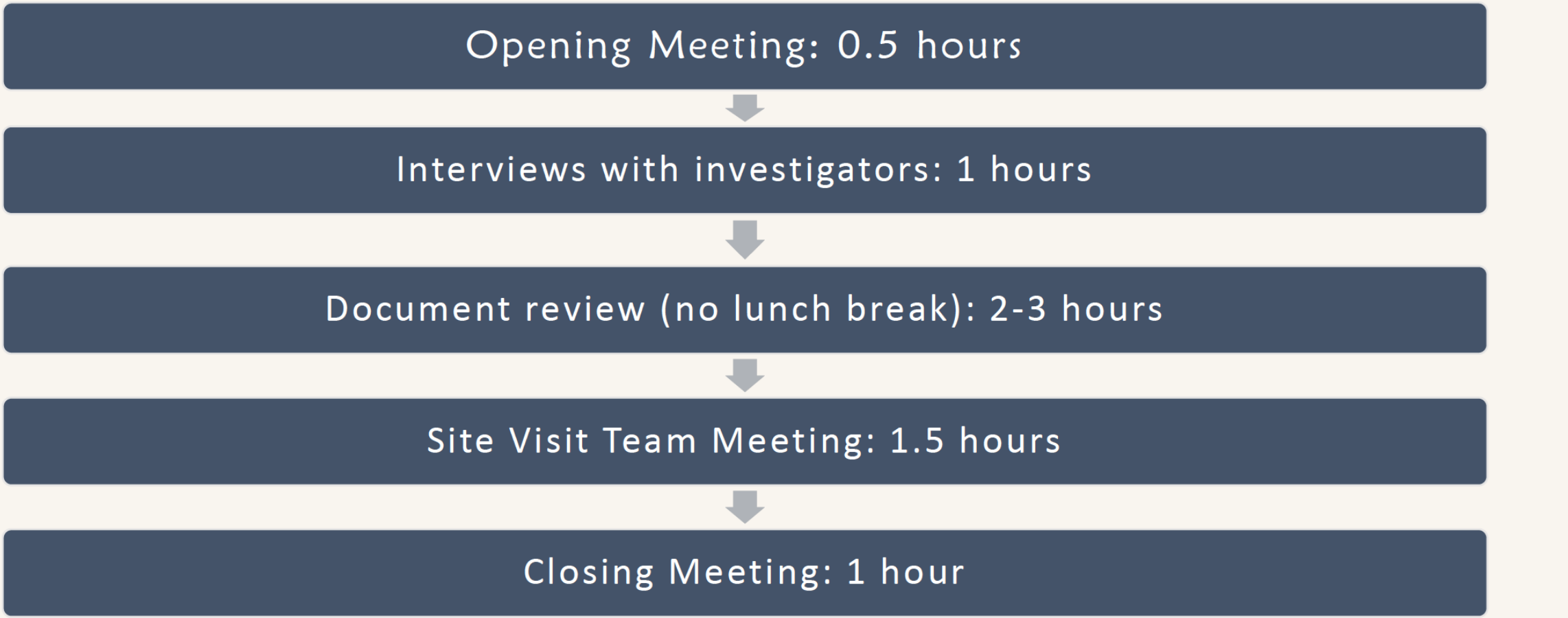
- Security, privacy, confidentiality of the documents at the study site.
- Facilities.
- Overall protection of the rights, safety and welfare of human participants.

# Closing out or Ending the Site Visit

At the end of the visit, the Site Visit Team will:

- Discuss the findings with the research team,
- Solicit feedback regarding the visit.

# Example of Conduct of Site Visit




From slide deck of Prof. Edlyn Jimenez

# Presenting the Site Visit Findings during the Full Board Meeting

- During the meeting, the Secretariat Staff distributes the completed Site Visit Report Form to the Panel Members along with the meeting agenda.
- The panel deliberates on the implications of results of the Site Visit on the rights, safety, and welfare of the study participants; and makes an overall determination of protocol compliance in the study site.
- Various other recommendations should be made depending on the reasons for the site visit.

# Communication of Results

- The PI is notified of the panel action or recommendations through an action letter.
- The PI may be requested to provide additional information, submit additional documents, or implement corrective action.

# SOP: Site Visit Workflow

| ACTIVITY | RESPONSIBLE PERSON |
|---|---|
| Select study sites to visit<br>↓ | UPMREB Chair, Panel Chairs, Panel Secretaries, and Members |
| Notify PI of date of "site visit"<br>↓ | Panel Chair and Panel Secretary |
| Create Site Visit Team<br>↓ | Panel Chair and Panel Members |
| Conduct Site Visit<br>↓ | Site Visit Team |
| Present findings during panel meeting<br>↓ | Panel Chair |
| Communicate results of Site Visit and subsequent panel action to PI<br>↓ | Secretariat Staff |
| Manage Site Visit documents | Secretariat Staff |

**University of the Philippines Manila**
**RESEARCH ETHICS BOARD**
2nd Floor Paz Mendoza Building, College of Medicine, UP Manila
547 Pedro Gil Street, Ermita, 1000 Manila
*Telephone*: +63 2 5222684; *Mobile*: +63 927 3264910; *Email*: upmreb@post.upm.edu.ph

< dd/mm/yyyy>

**<NAME OF PANEL MEMBER>**
Panel Member
<Review Panel>

**Re: <STUDY PROTOCOL TITLE> <UPMREB CODE>**
Dear **<TITLE OF PANEL MEMBER> <SURNAME>**:

We wish to inform you that the UPMREB has appointed you to be a member of the Site Visit Team responsible for verifying compliance of the study site with UPMREB approved protocol and related documents, such as, contents of the informed consent form, etc. This site visit is being organized because of: _____. As part of the team, your responsibilities include the following:

1. Review the study protocol and the ICF (note: make sure that the site is using the most recent version)
2. Review the post-approval documents (note: make sure that the site is using the most recent version)
3. Ask the PI or staff to explain the informed consent process
4. Ensure security, privacy, and confidentiality of the documents at the study site
5. Discuss the findings with the research team
6. Solicit feedback from the study site

The details of the Site Visit are as follows:

| | |
|---|---|
| **Study Site** | |
| **Address** | |
| **Date** | <dd/mm/yyyy> |
| **Time** | <hh:mm> |

UPMREB FORM 3(H)2012: NOTICE OF SITE VISIT
23/09/2021

To facilitate the intended site visit, please signify your confirmation by signing in the space provided below, date your signature, and return one copy of this letter to the UPMREB Secretariat. Also, if you have any questions regarding the information outlined in this notification, you may visit the UPMREB Secretariat at the UPMREB Office, email upmreb@post.upm.edu.ph, or call telephone number +63 2 5222684 for assistance.

Thank you and best regards.

Very truly yours,

Name and Signature
Chair, UPMREB Panel

Name and Signature
CONFORME of Panel Member
DATE SIGNED: <dd/mm/yyyy>

# Sample of Site Visit Notification Template

**RECOMMENDED ACTION:** (For UPMREB use only)

- ☐ NO FURTHER ACTION
- ☐ REQUEST INFORMATION: (specify)
- ☐ RECOMMEND FURTHER ACTION: (specify)
- ☐ PENDING, IF MAJOR CLARIFICATIONS ARE REQUIRED BEFORE A DECISION CAN BE MADE

| | | | |
|---|---|---|---|
| **PRIMARY REVIEWER** | | Signature | |
| Date: <dd/mm/yyyy> | | Name | <Title, Name, Surname> |



UPMREB FORM 3(F)2012: SITE VISIT REPORT FORM
02/09/2022

**t previously reported to the**

**ecured adequately?**

**(e.g. advertisements) used in**

**could affect participant's/subject's**

**ction for the rights, safety or**

**?**

**this site visit?**



**Sample of Site Visit Report Template**

| Activity | Documentation | Interview | Observation |
|---|---|---|---|
| 1. Regulatory documents | • Approvals: REC, FDA (?)<br>• Case report forms<br>• Data collection forms<br>• Valid practicing licenses<br>• Study brochures | • If approval is valid<br>• Communication with collaborators | • Availability of study related documents |
| 2. Facilities | • Recruitment areas<br>• Clinics<br>• Laboratories<br>• Dispensing areas,<br>• Storage facilities for drugs and other study materials,<br>• Data management areas,<br>• Study staff<br>• Record offices | • How many studies are being conducted at the site<br>• Approval status<br>• Number of staff for the study | • Availability and the amount of space compared to the participant population<br>• Approval letters<br>• Available staff (site delegation log) |

| Activity | Documentation | Interview | Observation |
|---|---|---|---|
| 3. Informed consent process and documentation | • Signed informed consent forms | • How it is obtained<br>• Who witnesses<br>• How long it takes | • Observe the process of obtaining consent |
| 4. Participant welfare | • Amount approved in consent form<br>• Signature of recipient | • How much is given<br>• How is the amount determined<br>• Who gives out the cash<br>• Ask participant what they get | |
| 5. SAEs management and reporting | • Records of identified SAEs and their management<br>• Signed SAE reports | • How identified<br>• How managed<br>• Status of the SAE | SAE reports |

| Activity | Documentation | Interview | Observation |
|---|---|---|---|
| 6. Study related training | • Training certificates | • When trained<br>• Who trained<br>• Importance of the training<br>• Knowledge of regulations and study protocol | • Ability to perform as trained |
| 7. Working Practices | • Minutes of meetings<br>• Communication memos<br>• Communication with collaborators<br>• Availability of SOPs<br>• Delegation logs | • Frequency of meetings<br>• What is discussed in the meetings<br>• How long the meetings take<br>• Explaination of procedures | • Meeting minutes<br>• SOPs at work stations |

Ochieng et al. BMC Medical Ethics 2013, 14:23
http://www.biomedcentral.com/1472-6939/14/23

BMC Medical Ethics

RESEARCH ARTICLE Open Access

# Research site monitoring for compliance with ethics regulatory standards: review of experience from Uganda

Joseph Ochieng[1*], Julius Ecuru[2], Frederick Nakwagala[3] and Paul Kutyabami[4]

- 25% of the reports showed violation of the regulatory requirement for valid ethical approval.
- 36% informed consent violations,
- 28% violation of the rights and welfare of research participants,
- 38% revealed that sites did not report SAEs to regulatory authorities and
- Many sites lacked adequate GCP and GLP.
- However, most of the sites monitored had **adequate facilities** to conduct the respective studies and good working practices.

# ICF Process Violations (36%)

1. Consent was not obtained, or there was no adequate documentation to prove that informed consent had been obtained.
2. Incomplete consent forms, for example, some pages missing.
3. Using study staff to witness consent for illiterate participants
4. Unsigned consent forms which could imply that an investigator may have missed reviewing the consent as required by their own protocol,
5. Lack of separate consent for stored specimen.

Ochieng *et al. BMC Medical Ethics* 2013, **14**:23
http://www.biomedcentral.com/1472-6939/14/23

Ochieng et al. BMC Medical Ethics 2013, 14:23
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# Participant Welfare (28%)

1. Participants were either not compensated for their time or got inadequate compensation.
   - For example, participants waited for long periods without a snack or a meal and were not compensated for time and work lost. In one scenario, participants who normally would not require hospital admission were admitted for more than one week in order to participate in a clinical trial yet no compensation for time lost was done.
2. However, many of the studies that did not adequately compensate the participants had been approved in that form indicating that the ethical review process had approved the protocol without due consideration for participant welfare.

# Summary

- Site visits from the ethics committee is a way to monitor the conduct of research for any study for which an approval has been issued by the REC;
- Part of the larger mechanism of continuing review and oversight.
- The most important points to determine are the activities, criteria, and other defining characteristics that qualify a site  for a visit and the corresponding action by the panel.