THE VITAL ROLE OF COMMUNITY RECRUITERS IN VACCINE TRIALS – CHALLENGES AND REAL-WORLD SOLUTIONS IN A UNIVERSITY RESEARCH CENTER IN THE PHILIPPINES

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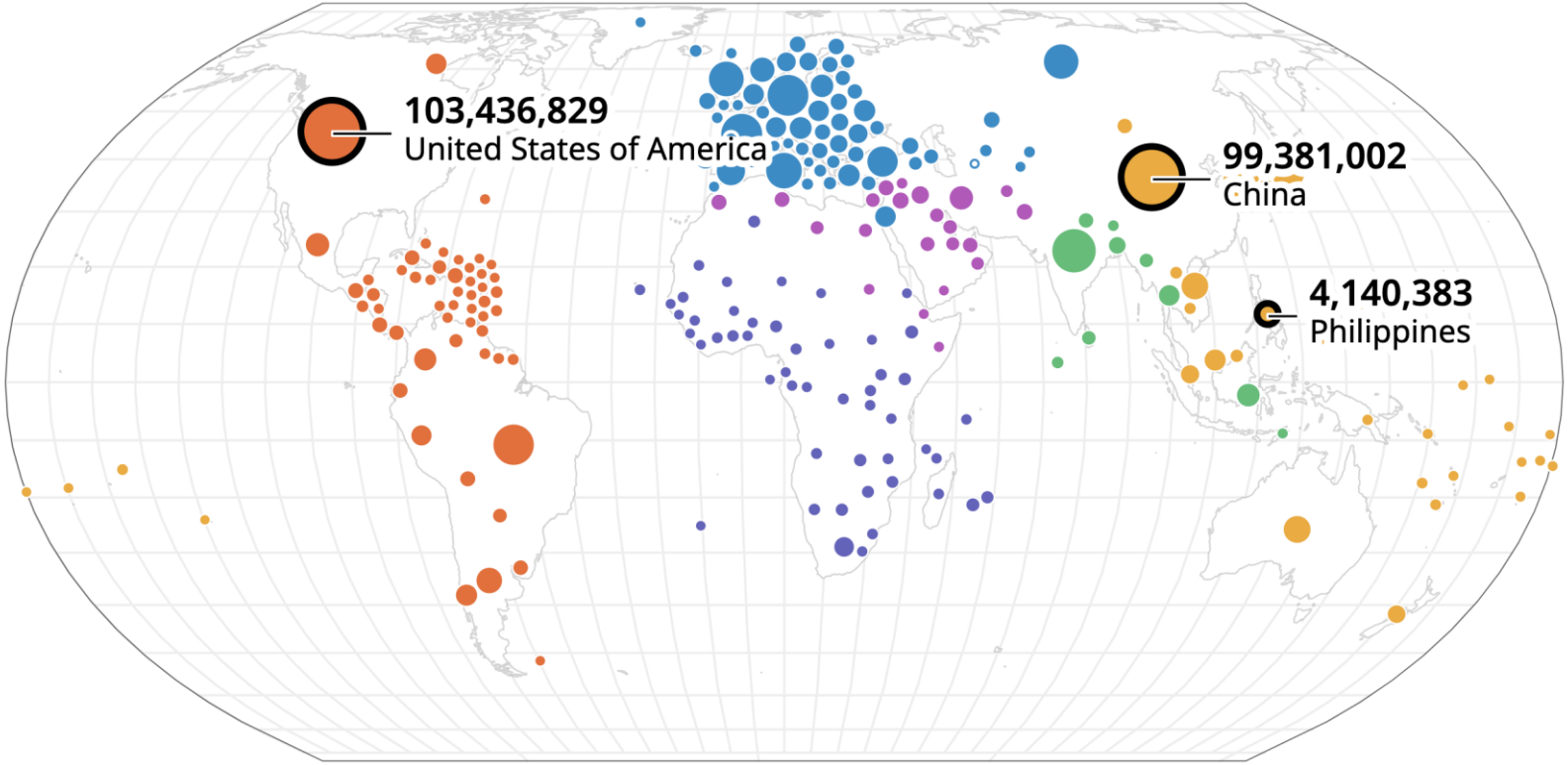
University of the Philippines – Philippine General Hospital

Objective

to share our experience in responding to a subset of **irregularities** in clinical trial subject recruitment that is not separately addressed in the **good clinical practice (GCP)** framework.

The COVID-19 Pandemic

Trials that require enrollment of a high number of subjects within a short period of time



Number of COVID-19 cases reported to WHO (cumulative total)

https://data.who.int/dashboards/covid19/cases

History

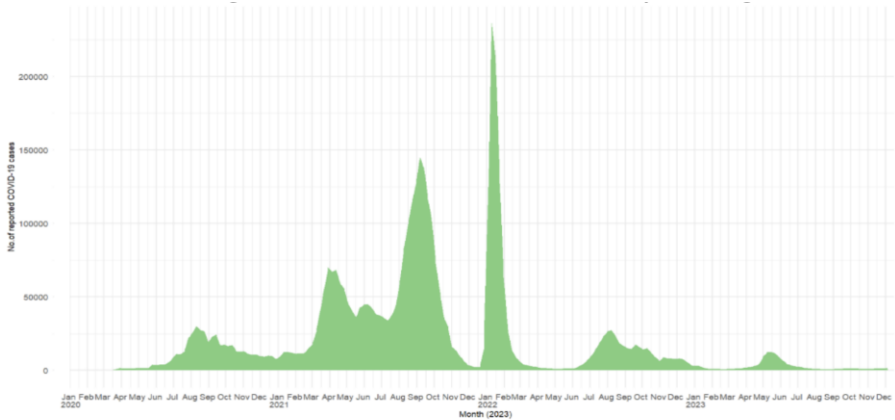


Figure 1. Daily reported COVID-19 cases in the Philippines (30 Jan 2020 -10 Dec 2023)

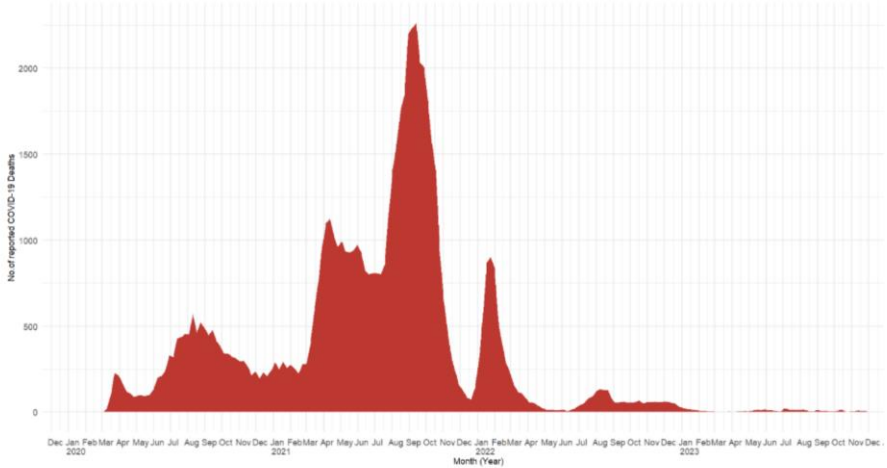


Figure 4. Daily number of COVID-19 deaths in the Philippines by date of death (30 Jan 2020 - 10 Dec 2023)

Please see the Philippines Department of Health (DOH) Daily Case Bulletins and COVID-19 Tracker for further information.

Summary of the epidemiological situation in Philippines[1]

COVID-19 deaths

As of 10 Dec 2023, 66,779 COVID-19 related deaths have been reported in Philippines since the beginning of the COVID-19 pandemic (Figure 4).

World Health Organization Philippines

Philippines
Coronavirus Disease 2019 (COVID-19)
Situation Report #142

Data reported by the Department of Health on 11 Dec 2023

Press Statement || Updates on Applications for Conduct of Clinical Trials and Emergency Use Authorization of COVID-19 Vaccines

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The Food and Drug and Drug Administration (FDA) continues to accept applications for the conduct of COVID-19 Vaccine clinical trial (CT) in the Philippines. To date, FDA has received three (3) applications which underwent review and assessment of the Department of Science and Technology – Vaccine Expert Panel (DOST-VEP) and the Single Joint Ethics Review Board (SJREB).

On 28 December 2020, the FDA has granted approval for the conduct of CT on COVID-19 vaccine developed by Janssen Vaccines & Prevention B.V. The FDA also approved the clinical trial for the vaccine developed by Clover Biopharmaceuticals AUS Pty Ltd. today, 08 January 2021. "The FDA is currently awaiting response to clarifications for the proposed study on the Sinovac Life Sciences vaccine before issuing a decision on the application", Director General Eric Domingo said.

Acceptance and review of applications for Emergency Use Authorization (EUA) of COVID-19 vaccines is also underway. Evaluation of Pfizer-BioNTech COVID-19 Vaccine and AztraZeneca Pharmaceuticals-ChAdOx1-S (recombinant) COVID-19 Vaccine is ongoing. DG Domingo stated that the decision of approval is expected to be released within 21 calendar days upon filing of application

The EUA application for Sputnik V developed by Gamaleya National Center of Epidemiology and Microbiology-Ministry of Health Russia was received on 07 January 2021. "The submission was pre-assessed and the applicant was instructed to comply with the lacking documents," DG Domingo ended.

Attachment:-> JANUARY 8 2020 PRESS STATEMENT

28 December 2020 - Janssen Vaccines & Prevention B.V.

08 January 2021 - Clover Biopharmaceuticals AUS Pty Ltd.

https://www.fda.gov.ph/press-statement-updates-on-applications-for-conduct-of-clinical-trials-and-emergency-use-authorization-of-covid-19-vaccines/

COVID-19 Vaccine Clinical Trials in Philippines

Protein Subunit
Clover
SCB-2019
15 trials in 13 countries

Protein Subunit
EuBiologics Co Ltd
EuCorVac-19
4 trials in 3 countries

Protein Subunit
Jiangsu Rec-Biotechnology Co Ltd
ReCOV
6 trials in 3 countries

Protein Subunit
Livzon Mabpharm Inc
V-01
Approved in 1 country
7 trials in 3 countries

Protein Subunit
SK Bioscience Co Ltd
SKYCovione
Approved in 1 country
7 trials in 6 countries

Protein Subunit
West China Hospital
Recombinant (Sf9 cell)
9 trials in 5 countries

DNA
Inovio
INO-4800
10 trials in 9 countries

Non Replicating Viral Vector
Janssen (Johnson & Johnson)
Jcovden
Approved in 113 countries
26 trials in 25 countries

Non Replicating Viral Vector
Oxford/AstraZeneca
Vaxzevria
Approved in 149 countries
73 trials in 34 countries

Replicating Viral Vector
Wantai
DelNS1-2019-nCoV-RBD-OPT1
5 trials in 3 countries

Inactivated
KM Biologics Co Ltd
KD-414
7 trials in 2 countries

Inactivated
Sinopharm (Beijing)
Covilo
Approved in 93 countries
39 trials in 18 countries

Inactivated
Sinovac
CoronaVac
Approved in 56 countries
42 trials in 10 countries

RNA
GlaxoSmithKline
CV0501
1 trial in 3 countries

COVID19 VACCINE TRACKER

https://covid19.trackvaccines.org/country/philippines/

Our Center

- The **national university hospital** and premier referral center
- The **biggest modern government tertiary hospital** in the Philippines, servicing more than 600,000 patients annually
- 1,100 public beds and 400 private beds
- Remains the **only national referral center for tertiary care**, providing direct and quality patient services to thousands of indigent Filipinos all over the country.
- Functions:
  - Service
  - Training
  - Research

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PGH
PHILIPPINE GENERAL HOSPITAL
1907

UP-PGH

https://www.upm.edu.ph/pgh/

COVID-19 Vaccine Trials

318 participants

ENSEMBLE 2 Trial (VAC31518COV3009)

Participants: healthcare professional volunteers from PGH; **Word-of-mouth recruitment**

3200 participants

SARS-CoV-2 Vaccine (Vero Cells), Inactivated (2021L001)

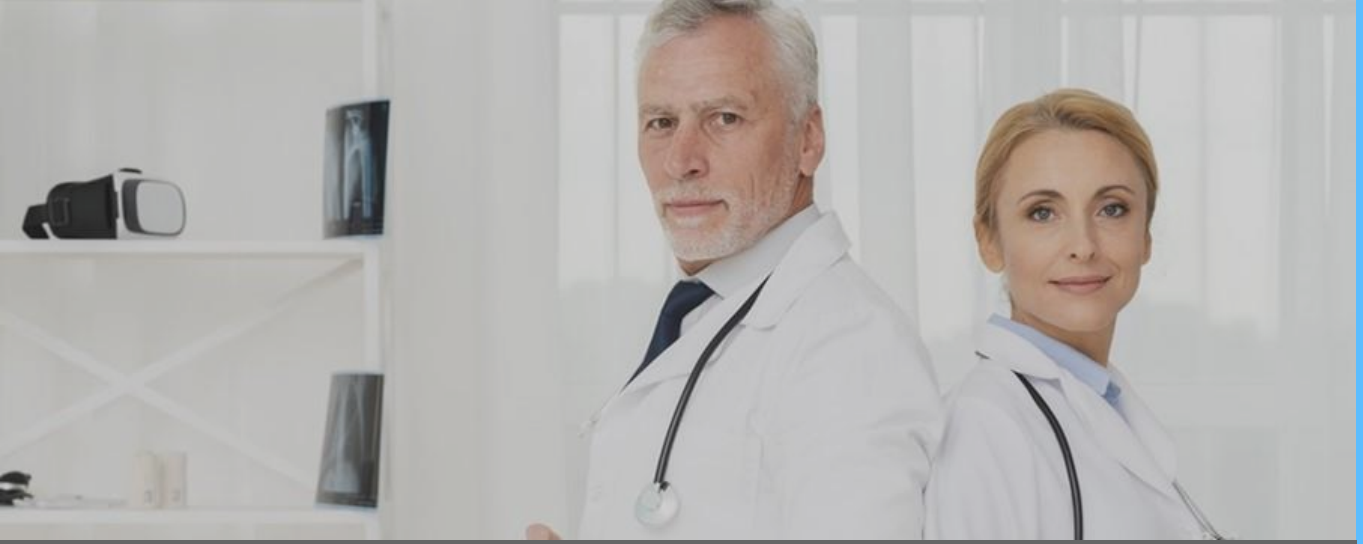
Participants: volunteers from nearby **communities** in Manila coordinated by a **community recruiter and sub-recruiter/s**

COVID-19 Trials Conducted at PGH

	**318 participants**	Phase 3 Study of recombinant, replication-incompetent adenovirus type 26 (Ad26) vector Ad26.COV2.S (ENSEMBLE 2) (Protocol VAC31518COV3009)
	**3,200 participants**	Phase 3 Study of SARS-CoV-2 vaccine (Vero Cells), Inactivated (Protocol 2021L001)
	**3,557 participants**	Phase 3 Study of influenza virus vector COVID-19 vaccine for intranasal spray (DelNS1-2019-nCoV-RBD-OPT1) (Protocol COVID-19-PRO-003)
	**1,717 participants**	Phase 3 Study of SARS-CoV-2 variant BA.4 /5 mRNA vaccine ABO1020 (Protocol ABO1020-301)
	**150 participants**	Phase 2 Study of immunogenicity of the recombinant two-component COVID-19 vaccine (CHO cell) (Protocol REC611C301)

Other Ongoing Trials Conducted at PGH

	**862 participants**	Phase 3 Study on PIKA Rabies Vaccine (Vero Cell) for Human Use, Freeze-dried in Healthy Adults using a Post-Exposure Prophylaxis schedule (Protocol YS-002)
	**310 participants**	Phase 3/3b Study on MF59-Adjuvanted Quadrivalent Subunit Inactivated Influenza Vaccine Compared to a Quadrivalent Influenza Vaccine (Protocol V118_24)



The New Clinical Trial Stakeholder:

The Community Recruiters And Sub-recruiters

Participant recruitment remains a critical factor that determines the successful completion of a clinical trial.

Community recruiter

/kəˈmjuːnəti//rɪˈkruːtə(r)/

- members of the community from where the trial will recruit

- in practice, they are not officially delegated as they are deemed as not having sufficient level of education for GCP training

- mostly motivated by financial gain

Community recruiter

- may be a barangay captain, barangay councilor, barangay health worker, or any person without official administrative position but with wide and strong network

*”They are mostly **motivated by financial gain**, sometimes internally arranging with their recruited subjects to be given a percentage of the subject compensation, based on anecdotal reports, which we endeavored to discourage through dedicated budgetary incentive allocated specifically for recruiters.”*

Problems that arose with clinical trial site's collaboration with the community recruiters:

Problem #1: Kickbacks or deductions on participant's travel allowance

Solution: Incentives to recruiters per participant enrolled

Problems that arose with clinical trial site's collaboration with the community recruiters:

Problem #2: Multiple trial enrolment of participants across different sites

University of the Philippines Manila
RESEARCH ETHICS BOARD
Room 126, National Institutes of Health, UP Manila 623 Pedro Gil Street, Ermita, 1000 Manila
Telephone: +63 2 8526-4346; Email: upmreb@post.upm.edu.ph

MEMORANDUM JVM—2024—01

17 May 2024

TO: ALL PRINCIPAL INVESTIGATORS

FROM: JACINTO BLAS V. MANTARING III, MD, MSC
UPMREB Chair

SUBJECT: Advisory Against Unscrupulous Recruiters

Please be advised that the University of the Philippines Manila Research Ethics Board (UPMREB) received a report that a recruiter for a clinical trial being conducted in another hospital attempted, on several occasions, to recruit from current subjects of an active clinical trial being conducted in the Philippine General Hospital. According to the report, this recruiter is soliciting the participation of subjects who are already enrolled in different clinical trials, with offers of assistance in falsifying documents to meet eligibility requirements of the trial in that other hospital. In the interest of protecting the well-being of clinical trial subjects, **all Principal Investigators are instructed to**:

MEMO from local IRB
17 May 2024

1. Establish appropriate **site control procedures** for detecting false documents that may be used in the enrolment of the subjects.

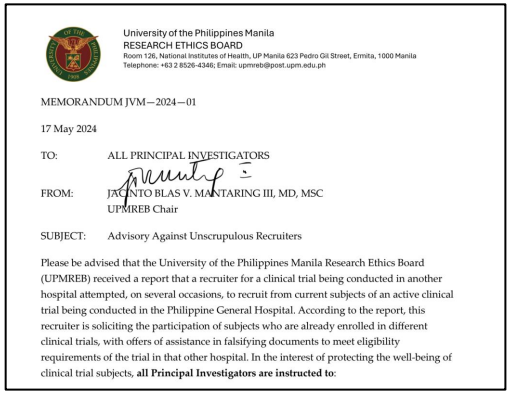
2. **Contact respective clinical trial subjects** to warn them against such predatory recruitment practices and the dangers posed by multiple clinical trial enrolment.

3. Create vetting procedures for community recruiters, if respective clinical trials are using such services, and **formally accredit these recruiters' affiliation with the clinical trial site to facilitate accountability**; and submit an amendment to site specific procedures.

4. **Closely monitor** any future similar occurrences encountered.

5. **Continue to report** all such occurrences encountered immediately

6. **Submit parallel notifications** to the Single Joint Review Ethics Board (SJREB), for clinical trials under SJREB oversight.



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Other Action from UPMREB

Meeting with clinical trial stakeholders (Principal Investigators, Sub-investigators, Study Coordinators, Sponsors, clinical/contract research organizations (CRO)) from various ongoing studies conducted in UP-PGH

- Future plan on **shared database** of all participants enrolled in clinical trials to prevent multiple enrolment
- Strong recommendation: **Training** of all community recruiters and **formal delegation** as study site staff

Site's response

NOTIFICATION

22JULY2024

Dear Dr. De Jesus and other members of UPMREB Panel 2:

Due to the recent reports of clinical trial participants being discovered who simultaneously enroll in different clinical trials for various reasons, and other circulating reports of fraudulent transactions and falsified documents (i.e. ID cards and birth certificates), our site decided to urgently contact individually our active participants in the above-mentioned trial to verify from the subjects themselves that they are not in any way involved in multiple clinical trials, multiple sites (of the same trial), and any fraudulent activity in relation to their participation in this current study.

We believe that participating in multiple clinical trials will seriously compromise participant safety, and data integrity of the study. In the event that cross-enrollees will be detected through this call, we will immediately report them to you and to the sponsor and recommend the following actions:

1. Continuous participant follow-up for safety monitoring purposes
2. Removal of the subject in the efficacy analysis of the study

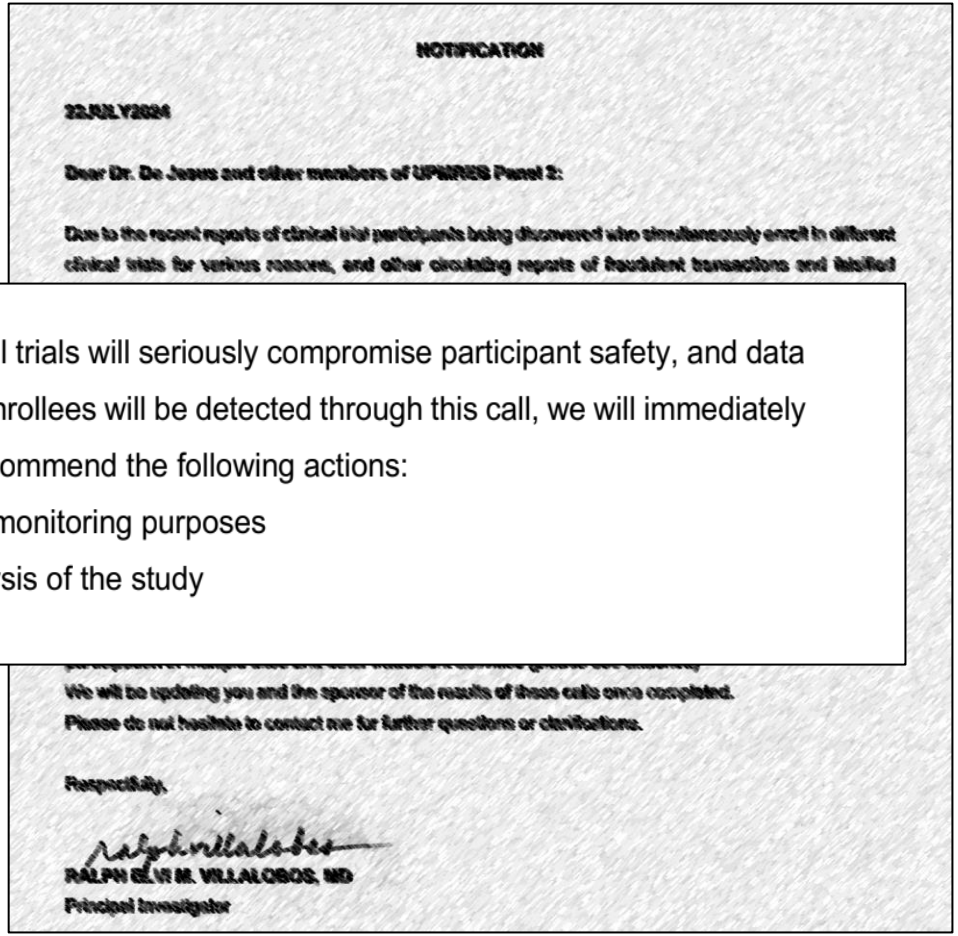
We used a site-specific and site-initiated generic script containing specific questions that are related to participation in multiple sites and other fraudulent activities (please see attached)
We will be updating you and the sponsor of the results of these calls once completed.
Please do not hesitate to contact me for further questions or clarifications.

Respectfully,

ralphvillalobos

RALPH ELVI M. VILLALOBOS, MD
Principal Investigator

Site’s response



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2. Removal of the subject in the efficacy analysis of the study

Site's Actions

Site's initiative to urgently contact participants individually in two (2) ongoing clinical trials to verify enrolment in multiple clinical trials, multiple sites (of the same trial), fraudulent activities.

Questions:

*1. Are you **currently/or planning to participate in another clinical trial** for whatever indication, aside from the study you are currently enrolled in?*

*2. Are you also **currently involved in the same clinical trial conducted in other sites**?*

*3. Are you personally **involved in any fraudulent/potentially fraudulent activity** related to your participation in this clinical trial (e.g. falsification of ID cards, fabrication of any information)?*

*4. Are you, to the best of your knowledge, **aware of any fraudulent activities** committed by other individuals in relation to this clinical trial (e.g. community recruiter-initiated fraudulent schemes like falsification of documents, monetary extortion, etc.)?*

Problems that arose with clinical trial site's collaboration with the community recruiters:

Problem #2: Multiple trial enrolment of participants across different sites

Solutions (other site's actions):

1.) Recruiters to sign a binding contract only to work for our site

2.) File an affidavit to avoid these fraudulent activities

3.) Training program

- A. Good Clinical Practice (GCP)
- B. Study protocol
- C. Community coordination

4.) Including them in the documented delegation of clinical trial responsibilities

Problems that arose with clinical trial site's collaboration with the community recruiters:

Problem #3: Falsification of trial participant's documents (i.e. government-issued IDs, birth certificates)

Solutions:

1.) Update site's SOP to detail strict policy on requiring participant to provide at least two IDs verifying them using verification apps (QR code), physical/visual testing, or other means, sometimes with the assistance of verified recruiters.

2.) With IRB's approval and instructions: revisited enrolled participant profiles to identify any suspicion of irregularity

1. Will serve exclusively as the community coordinator at clinical trial site UP–Philippine General Hospital and shall not engage in any recruitment or coordination activities for any other clinical trial site or other community recruiter, whether directly or indirectly;

2. Coordinating with the site the list of requirements and the schedule of visits of the said participants, as well as reminding them of their next scheduled visits;

3. Coordinate with the site regarding patients who cannot be reached/contacted in surveillance visits.

Functions of the Community Recruiter

Salamat po.

Thank you.

Do you have any questions?

Orlie John Lavilla, MD
orlie.lavilla@gmail.com

Ralph Elvi Villalobos, MD
ralphvillalobos1987@gmail.com

https://www.upm.edu.ph/pgh/