Subject Recruitment

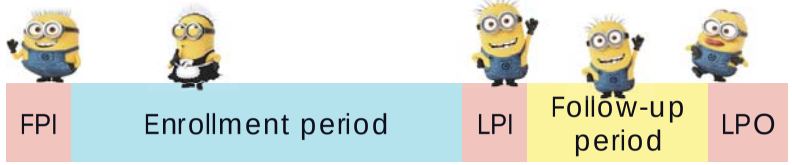
Recruit Subjects as Committed

- The investigator should be able to demonstrate a potential for recruiting the required number of SUITABLE SUBJECTS within the AGREED RECRUITMENT PERIOD

- Meet the enrollment target
- Recruit SUITABLE SUBJECTS
  - o Inclusion criteria
  - o Exclusion criteria

❑ Meet recruitment timeline (Recruitment/enrolment period)

Recruitment Period



- First patient in (FPI) or first patient first visit (FPFV)
- Last patient in (LPI) or last patient first visit (LPFV)
- Last patient out (LPO) or last patient last visit (LPLV)

Subject Recruitment (การคัดเลือกอาสาสมัคร)

Recruitment phase
(ระยะของการคัดเลือกอาสาสมัคร)

Pre-screening
(ระยะก่อนคัดกรอง)

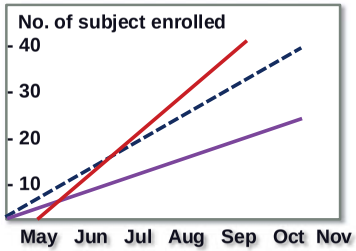
Screening
(คัดกรอง)

Enrollment
(เข้าร่วม)

Randomization
(สุ่มเข้ากลุ่มวิจัยหรือเปรียบเทียบ)

Subject Recruitment

- Recruitment process
  - A. Develop recruitment strategic plan and contingency plan before study started
  - B. Get started:
    - Set recruitment goal and timeline
    - Develop tracking tool
      - o screening/ recruitment log
  - C. Run the operation
  - D. Motivate team



Screening Log: an example

Protocol ID:							
Investigator Name: Site ID:							
Subject Screening ID	Date of Consent	Date Screened	Reason for Screen Fail	Date Re-Screened (if allowed)	Reason for Screen Fail	Date Enrolled	Subject ID

Recruitment strategies

OBJECTIVE:

- To enroll interested, eligible and informed subjects in a manner that respect their privacy and autonomy

HOW

I. Identify target population

- Eligibility criteria
- Demographic & epidemiological data
- Diagnosis, treatment & referral pattern
- Competing studies

Recruitment strategies

HOW

II. Choosing strategies

- Sources:
  - Hospitals (primary, secondary, or tertiary care); and clinic
  - Laboratories
  - Community
  - Medical record
  - Others: school, military facilities, etc.

Recruitment strategies

HOW

III. Choosing strategies

- Strategies
  - Chart/record review
  - Referral:
    - formal
    - informal (word-of-mouth)
  - Community screening
  - Advertising:
    - mass media, mass mailing,
    - local announcements (bulletin board),
    - advocacy group, support group meeting

Recruitment strategies

HOW

II. Choosing strategies: factors should be considered

- Accessibility
- Yield of eligible subjects
  - Volume & flow of screenees
  - Screening failure rate
- Cost VS Yield
- Special (vulnerable) population: women, minorities, elderly

Recruitment strategies

HOW

III. Develop contingency plan or back-up strategies

- Ability to shift rapidly from unsuccessful recruitment strategies

Recruitment strategies

HOW

IV. Methods that involve direct communication to subject

- must be reviewed and approved by IRB/IEC
- Should not INDUCE / PERSUADE and COERCIVE / FORCE

V. Assure protocol compliance

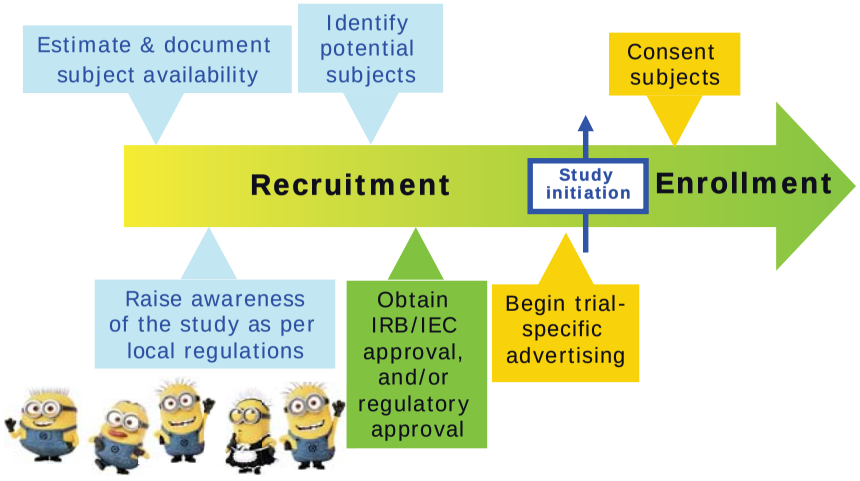
Recruitment strategies

HOW

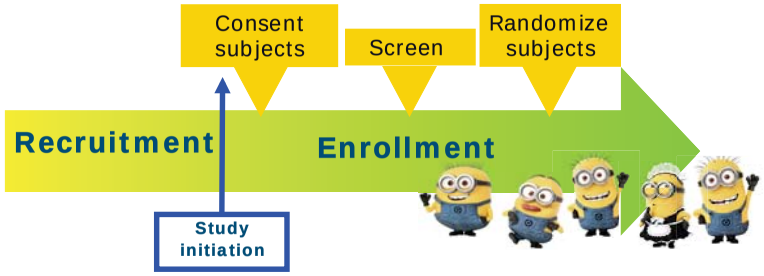
VI. Determine timing of informed consent

- Prior to any study procedures, no screening with invasive testing can be completed before informed consent

Recruitment process



Enrolment process



- Prior to the beginning of the trial, the investigator should have the IRB/IEC's written approval/favorable opinion of
  - Written informed consent form and
  - Other written information provided to subjects.

Key things to remember

- Timely recruitment of eligible subject is crucial
- Develop recruitment plan and contingency plan before study started
- All materials communicated directly to subjects must be approved by IRB/IEC before use
- Recruit subjects in accordance with protocol
- Monitoring the rate of enrollment is essential
- Motivate team

Investigation group

Control group

Randomization & Maintenance of Randomization Code

Randomization

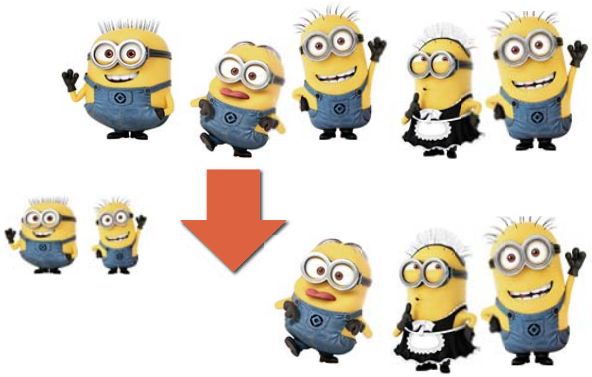
DEFINITION

- A process that assigns the subject by chance, rather than by choice, to either the investigational group or the control group
- To reduce biases
  - Each subject has a fair and equal chance of receiving either investigational intervention or control intervention
- To produce comparable groups
  - General characteristics
  - Demographics: age, gender,
  - Other key factors that affect the probable course the disease would take

Randomization

Investigator SHOULD

- follow the trial's randomization procedures
- keep randomization code in a secure place
- ensure that the code is broken only in accordance with the protocol
- If the trial is blinded,
  - promptly document and explain any premature unblinding to the sponsor and IRB/IEC (if required)



Subject Retention

Patient Retention

- Patient Retention
  - Most difficult and challenging
  - Key success of clinical trial

- Loss of study data: not be able to accurately evaluate safety and efficacy of study drug
  - An effective medication may look ineffective
  - An ineffective medication looks effective
  - Failure to detect a drug-related safety issue

Subject Retention

- Maximizing retention in clinical trial
  - A successful trial is a partnership between the subjects and the investigative staff.
  - The partnership is based on
    - Respect
    - Courtesy
    - Honesty
    - Listening carefully
    - Communicate openly

Subject Retention

- Maximizing retention in clinical trial
  - Investigative staff need to work closely with subjects both before and during study
  - Stay to contact with subjects
    - At least monthly if the study is long-term
    - Make reminder telephone call the day before a scheduled visit

Subject Reten

Must be reviewed & approved by IRB/IEC

- Maximizing retention in clinical t
  - Say thank you,
    - also thank them in other ways (e.g., sending birthday card, thank you note
  - Pay attention to subject's special needs
    - Transportation
    - Childcare
  - At each visit ask if subjects have any concerns or questions

Subject Retention

- Maximizing retention in clinical trial
  - Ensure that staff maintain patient confidentiality
  - Ensure that staff are
    - Friendly
    - Enthusiastic
    - Professional

- Patient who volunteer for studies are special persons. They should be treated as such

Key things to remember

- Loss of study data may compromise accuracy and reliability of the study results
- Therefore retention of subjects is crucial.
- Respect, courtesy, honesty, listening and open communication are key factors in subject retention
- Stay contact with subjects

Protocol compliance

Protocol Compliance

Investigator

- SHOULD
  - conduct the trial in compliance with the approval protocol
  - sign the protocol or an alternative contract, to confirm this agreement

(Ref. ICH GCP 4.5.1 – 4.5.4)

Protocol Compliance

- SHOULD NOT make any deviation from, or changes of the protocol
  - without agreement by the sponsor
  - prior review and approval from the IRB/IEC,
  - EXCEPT
    - to eliminate an immediate hazard to trial subjects,
    - the change involves only logistical or administrative aspects of the trial

(Ref. ICH GCP 4.5.1 – 4.5.4)

Protocol Compliance

- SHOULD ASSURE compliance with the protocol
  - inclusion & exclusion criteria
  - study drug administration & inhibited concomitant medication
  - study procedures e.g.,
    - scheduled visit,
    - outcome measurements, lab test
    - safety reporting
  - recording

Protocol Compliance

- Consequences of non-compliance
  - adversely affect scientific validity of the research
  - data lost
    - compromise scientific integrity of study
    - create statistical analysis problems
  - adversely affect safety, right and well-being of subjects
  - too many deviations attract audit/inspection
  - sponsor may not pay

Protocol Compliance

- Types of non-compliance
  - Protocol deviation
    - Minor protocol deviation
    - Major protocol deviation (Protocol violation)

Protocol Compliance

- Types of non-compliance
  1. intentionally decided to deviate
     - lab criteria, age criteria, pre-treatment criteria, payment,
  2. known before deviations occur, but cannot be prevented
     - subject cannot be at study visit; and not under investigator's control
  3. discovered after they occur

Ref. SACHRP Recommendation on Protocol Deviations; http://www.hhs.gov/ohrp/sachrp/mtgings/2012%20Feb%20Mtg/protocoldeviations.pdf (access 21 April 2013)

Protocol Compliance

- Causes of non-compliance
  - Investigator, site staff: intentional & unintentional
  - Subject's compliance
  - Unexpected circumstances: flooding
- Protocol deviation VS protocol amendment
  - Protocol amendment:
    - planned and systematic change
    - require IRB/IEC approval before implementing
  - Protocol deviation:
    - unplanned and isolated
    - serious and continuing deviation; study may need to be terminated

Protocol Compliance

HANDLING OF PROTOCOL DEVIATION

- Once protocol deviation/violation is known
  - report to sponsor and IRB/IEC (if required)
  - identify effects on risks to subjects and scientific quality of study and correct
  - identify root causes, and develop & implement action plan to prevent the future deviation
  - document

Subject compliance

Subject Compliance

- Develop strategies to maximize compliance
  - Adhering to visit schedule
    - Scheduling all subject visits at the initial visit
    - Use window period of each visits making appropriate appointment
    - Visit reminding is needed.

Subject Compliance

- Develop strategies to maximize compliance
  - Complying with the use of study drugs
    - dosing
    - frequency
    - contraindicated medications
    - return of medication
    - other requirements e.g., warning

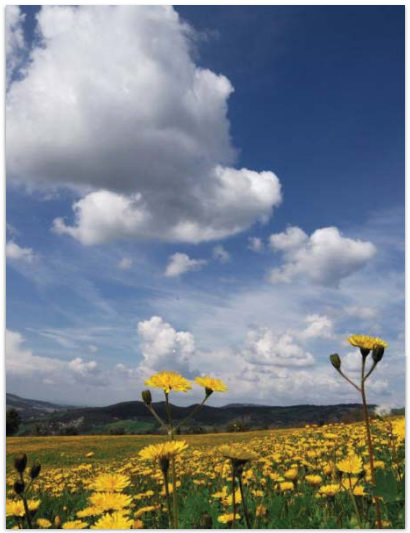
Subject Compliance

- Develop strategies to maximize compliance
  - Adverse event reporting
    - When and whom to report
    - Report use of concomitant drugs
    - Study participant card may be useful
  - Record keeping, e.g., diaries
  - Have correct contact details for subjects
- Know how to record non-compliance

Key things to remember

- Work closely with subjects to ensure their compliance to the study protocol

Provision of Medical Care to Trial Subjects



Medical care

- A qualified physician should be responsible for all trial-related medical decisions.

Investigator SHOULD

- ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial
- inform a subject when medical care is needed for intercurrent illness (โรคแทรกซ้อน)

Medical care

- Inform the subject's primary physician about the subject's participation in the trial
  - if the subject has a primary physician and
  - if the subject agrees to the primary physician being informed
- When the subject withdraws prematurely from a trial,
  - should make a reasonable effort to ascertain the reason(s),
  - while fully respecting the subject's rights