Clinical Research Ethics

Dr Yin Thet Nu Oo
M.B.,B.S Master of International Research Bioethics (Monash)
Hubert Humphrey Fellow (Emory University)
Deputy Director
Department of Medical Research

Research involving human participants

(sometimes termed “human subjects” in research protocols and reports)

when human beings:

- are exposed to intervention, manipulation, *observation*, or *other interaction* with investigators either directly or through alteration of their environment, or

- become individually identifiable through investigators’ collection, preparation, or use medical or other records or of biological material from human beings.

What is clinical trial?

- A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. (Ref: WHO Definition)

- Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.

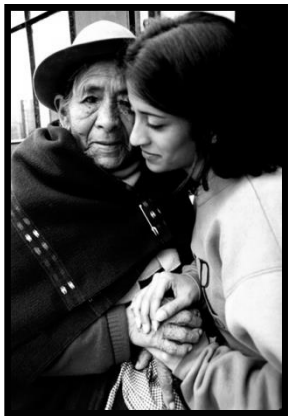
Case study

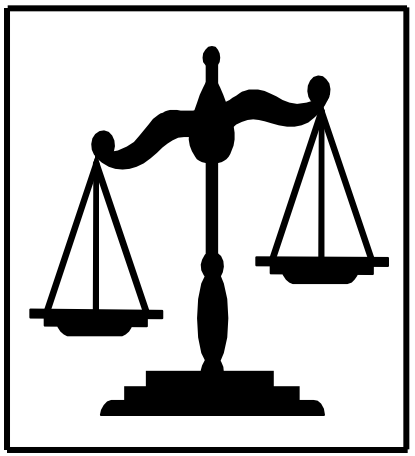
- Chris was recruited to participate in a clinical trial by his oncologist, Dr. Blair. Chris has cancer, and the traditional treatments have been only intermittently successful.
- The clinical trial is a randomized, single-blinded, placebo-controlled study of a drug that may be beneficial to patients with the kind of cancer that Chris has. The trial will last one year, and objective is to determine the efficacy of the new treatment.
- After six months in the study, Chris is not experiencing any signs of improvement, and he may in fact be getting worse. Dr. Blair continuously monitor the progress of the research subjects enrolled in both the treatment arm and in the placebo arm, and preliminary data seem to suggest that the drug is beneficial.
- During an examination Chris asks Dr. Blair if he is in the treatment arm or the placebo arm. Chris requests that if he is in the placebo arm Dr. Blair switch him to the treatment arm, so that he can receive the possible benefits of the new treatment. Dr. Blair knows that Chris is in the placebo arm.

- What should Dr Blair do in this situation?
- Does the patient has the right to know the arm he is in?
- When should the study stop?

Three Fundamental Principles of Research Ethics

- Respect for persons
- Beneficence
- Justice





Autonomy

auto - "self"
nomos - "rule", "law", "governance"
Self rule/self governance

Personal autonomy- self rule free from controlling interference by others & from limitations - inadequate understanding that prevent meaningful choices

Respect for Persons

Each individual:

- Is unique and free
- Has the right and capacity to decide
- Has value and dignity
- Has the right to informed consent

Who Are Vulnerable Persons?

- Minors, pregnant women, prisoners
- Persons with mental disabilities
- Persons who are illiterate or have limited formal education
- Persons with limited access to health services
- Women in some settings
- Refugees

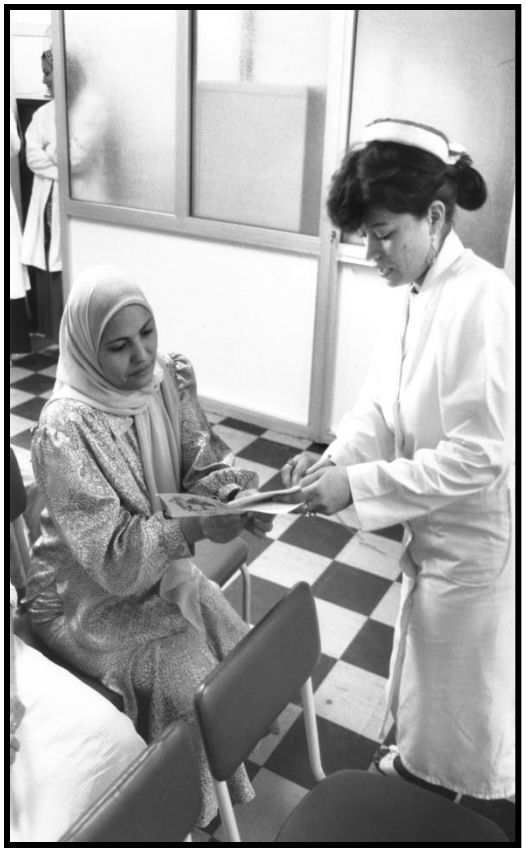





Beneficence

Researchers must:

- Protect physical, mental, and social well-being
- Reduce risks to a minimum
- Retain the community perspective



Nash Herndon/FHI

Beneficence (Cont)

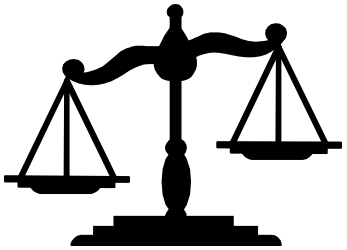
- Protection of the well-being of the participant is the primary responsibility of the researchers.
- Protecting participant is more important than:
  - the pursuit of new knowledge
  - the benefit to science
  - personal or professional research interest

Justice

Researchers must:

- Ensure a fair distribution of risks and benefits
- Conduct equitable recruitment of research participants
- Provide special protection for vulnerable groups

JUSTICE



Special protection for vulnerable groups

Justification for including a vulnerable group in research is when a problem disproportionately affects that group

The principle of justice forbids placing one group of people at risk solely for the benefit of another.

Eg : research conducted by developed country researchers in developing countries participant

(HIV prevention trials)

Ethical framework

- Valuable scientific question
- Valid scientific methodology
- Fair subject selection
- Favorable risk-benefit evaluation
- Independent review
- Informed consent
- Respect for enrolled subjects

Emanuel E, Wendler D, Grady C. What makes clinical research ethical? *Journal of the American Medical Association* 2000; 283(20):2701-11

Essential Elements of Ethical Research

Valuable Scientific Question:

Is the research question one that will generate new knowledge or understanding about human health or illness, i.e. a socially, clinically, or scientifically useful question

Essential Elements of Ethical Research

Valid Scientific Methodology:

Is the study designed in a way (design, methodology, statistical power and methods, etc.) that is feasible and will yield valid, reliable, generalizable, and interpretable data?

Essential Elements of Ethical Research

Fair Subject Selection:

- Selected for reasons of science and study purpose, not because of ready availability, vulnerability, or favor

- Consistent with scientific goals, selected so to minimize risks and maximize benefits, and fairly distribute research burdens and benefits

Essential Elements of Ethical Research

Balance of Risks and Benefits:

- Are risks to subjects necessary and minimized?
- Are risks justified by benefit to individual subjects and/or the importance of the knowledge to society?
- Are benefits maximized?

Essential Elements of Ethical Research

Independent Review:

Has the study received independent review to ensure that investigator biases have been checked, that ethical requirements have been fulfilled, and that subjects will not be exploited?

Essential Elements of Ethical Research

Informed Consent

Does the plan for informing participants about the objectives, risks, benefits, and alternatives of the study, assessing understanding, and seeking their voluntary agreement seem adequate?

Essential Elements of Ethical Research

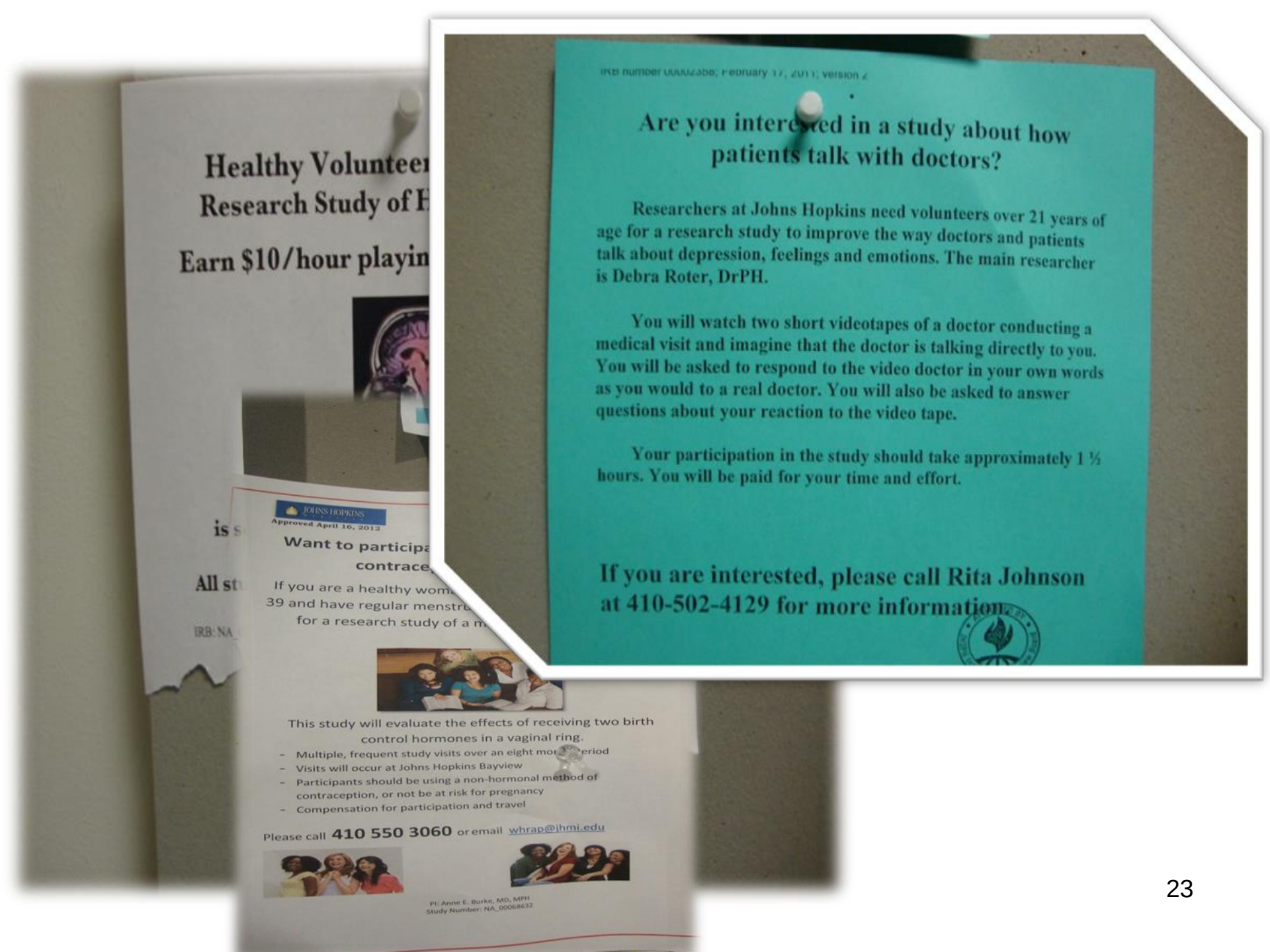
Respect for Enrolled Subjects

Are there adequate plans for respecting the rights and welfare of enrolled subjects during and at the end of the study?

For example, plans for protecting confidentiality of data, monitoring their welfare, informing them of new information and of study results, respecting their right to withdraw at any time?

Recruitment status

- **Not yet recruiting:** The study has not started recruiting participants.
- **Recruiting:** The study is currently recruiting participants.
- **Enrolling by invitation:** The study is selecting its participants from a population, or group of people, decided on by the researchers in advance. These studies are not open to everyone who meets the eligibility criteria but only to people in that particular population, who are specifically invited to participate.
- **Active, not recruiting:** The study is ongoing, and participants are receiving an intervention or being examined, but potential participants are not currently being recruited or enrolled.
- **Suspended:** The study has stopped early but may start again.
- **Terminated:** The study has stopped early and will not start again. Participants are no longer being examined or treated.
- **Completed:** The study has ended normally, and participants are no longer being examined or treated (that is, the last participant's last visit has occurred).
- **Withdrawn:** The study stopped early, before enrolling its first participant.
- **Unknown:** A study on ClinicalTrials.gov whose last known status was recruiting; not yet recruiting; or active, not recruiting but that has passed its completion date, and the status has not been last verified within the past 2 years.


Healthy Volunteer
Research Study of H
Earn $10/hour playin
JOHNS HOPKINS
Approved April 16, 2012
Want to participa
contrace
If you are a healthy wom
39 and have regular menstr
for a research study of a m
This study will evaluate the effects of receiving two birth control hormones in a vaginal ring.
- Multiple, frequent study visits over an eight mo period
- Visits will occur at Johns Hopkins Bayview
- Participants should be using a non-hormonal method of contraception, or not be at risk for pregnancy
- Compensation for participation and travel
Please call 410 550 3060 or email whrap@jhmi.edu
PI: Anne E. Burke, MD, MPH
Study Number: NA_00068632
Are you interested in a study about how patients talk with doctors?
Researchers at Johns Hopkins need volunteers over 21 years of age for a research study to improve the way doctors and patients talk about depression, feelings and emotions. The main researcher is Debra Roter, DrPH.
You will watch two short videotapes of a doctor conducting a medical visit and imagine that the doctor is talking directly to you. You will be asked to respond to the video doctor in your own words as you would to a real doctor. You will also be asked to answer questions about your reaction to the video tape.
Your participation in the study should take approximately 1 ½ hours. You will be paid for your time and effort.
If you are interested, please call Rita Johnson at 410-502-4129 for more information.

Informed Consent

What Is Informed Consent?

"Consent given by a competent individual who

- Has received the necessary information
- Has adequately understood the information
- After considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation"

Source: Council of International Organizations of Medical Sciences (CIOMS) Ethical Guidelines

Creation of Informed Consent Documents

- Use local language
- Write to appropriate reading level
- Illustrate with appropriate concepts and images
- Perform a translation and back-translation
- Pilot-test

Essential Elements of Informed Consent

1. Research description
2. Risks
3. Benefits
4. Alternatives
5. Confidentiality
6. Compensation
7. Contacts
8. Voluntary participation and withdrawal

Informed Consent

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. (1.28, ICH GCP 2016)

Informed consent is documented by means of a written, signed and dated informed consent form.

General Requirements

When obtaining consent from subjects for participation in clinical trials, the investigator must ensure that the following requirements are satisfied:

- Consent must be legally effective.
- The language used to obtain consent must be understandable to the subject (or the subject's LAR).
- Consent must be obtained under circumstances that allow the subject (or the subject's LAR) sufficient time to decide whether or not to participate.
- Consent must be obtained without undue influence or coercion.

Timing of Consent

- Once a subject is identified and agrees to participate in a trial, consent must be obtained. It is important that consent is obtained and documented before the subject's participation in the trial begins.

- However, procedures that are to be performed as part of the subject's medical care, and which would be done whether or not the participation in the trial were being considered, may be completed, without first obtaining informed consent from the subject.

Creation of Informed Consent

- Use local language
- Write to appropriate reading level
- Illustrate with appropriate concepts and images
- Perform a translation and back-translation
- Pilot-test

Documenting consent

- When the subject agrees to participate (or the subject's LAR agrees to the subject's participation) in the trial, consent is documented by having the subject (or the subject's LAR) personally sign and date the consent form.
- It is important that the person obtaining consent use the most current IRB/ERC approved version of the consent form.

- The FDA regulations require the subject (or subject's LAR) receive a copy of the consent form.
- ICH (2016) E6 Section 4.8.11 also requires that the subject (or subject's LAR) be given a copy of the signed and dated consent form.

Ethical consideration

- Please state how you consider the ethical issues as a scientist/researcher.
- How do you ensure confidentiality/ protect the privacy of participants
- How participants will be recruited?
- Process of getting informed consent
- Arrangement for consequences of your research (Eg., Proper referral and initial counseling for those who turned out to be HIV positive/ STI positive)
- Replication of the effective drug/intervention in the control group if applicable.

Ethical consideration

- okawoeusifhowfaumfrwDodkhwif_yppfaq;cHcJh_yD;/
- trnfemrrsm;udkvsdKhoSufxm;&Sd_cif;?
- vsdKhoSufxm;&Sd tyfaomtcsufrsm;udkvsdKhoSufay;_cif;?
- awG hqHkar;_ref;onfhae7m(vHk_cHKrSK&Sdap7ef?)
- wpfOD;csif;cGifh_yKcsufawmif;cH7ef?
- aus;Zl;wHkh_yefrSK
- 7&SdEdkifaomusef;rma7;oefaqmifrSKrsm;udkod&Sdvdkygu a_ym_ycJh7ef?

Ethical consideration

Concerning security of data, the following measures will be undertaken

- When data collection is all completed, completed observation checklist and questionnaire forms will be packed, sealed and carried by one of the research team members to the principal investigator's office. In the principal investigator's office, the assigned data entry staff will enter the data into the computer files which will be protected with computer code. After that, questionnaire forms will be kept under lock and key in the principal investigator's office. Only the principal investigator will have access to the data and questionnaire forms.

- The completed questionnaire forms will be kept for five years following publication.

- A 46-year-old man is currently enrolled in a Phase 2 study of a drug for severe diabetic neuropathy. While the study is on-going, a new drug becomes commercially available that may have equal or greater benefit to the subject. The investigator should do which of the following?

- **Give the subject comprehensive information about the new drug, including its side effects. Discuss the pros and cons of both the investigational drug and the commercially available drug and then allow the subject to decide whether to withdraw from the research to take the new drug.**
- **Withhold this new information to avoid confusing the subject with other treatment options or alternatives.**
- **Do not tell the subject about the new drug because physicians have the right to try out new treatments with their patients.**
- **Tell the subject about the new drug but discourage him from switching treatments until the study is completed.**

As part of a research study, a physician plans to review medical records to explore factors related to 50 of her patients who require (MRI) scans for clinical treatment.
The physician will review the medical records, and write down the clinical indication for the scans, any existing injuries, current prescriptions, as well as other clinical data.
The clinical indication for the scans and the other clinical data will be collected in the medical records .
The physician will use a coding system to be able to identify the patient's information and only she will have access to it. Which of the following is true?

- The study only requires IRB/ERC review if it is funded by government/MoHS.
- The study is human subject research which is eligible for expedited review.
- The study is human subject research which must be reviewed by the full IRB.
- The research does not meet the definition of human subject research.

When conducting a clinical study in accordance with Good Clinical Practice, which is the most important above all else?

- Protocol adherence
- Accuracy of data
- Protection of research participants
- Quality control/quality checks

How to submit for Ethics Review?

- Try to meet the requirements and formats of the ERC you plan to submit
- May submit to DMR ERC or other appropriate committees
- Submit your application about 2 months in advance of your data collection
- ERC needs adequate time to distribute the proposals to members so that they can give time for proper review

Continued learning

- ICH GCP training
- Research ethics online training(Global health training centre)

THE GLOBAL HEALTH NETWORK

WELCOME, YIN THET NU OO

Global Health Training Centre

What are you looking for? SEARC

Home | e-Learning Courses | Professional Development | Community | Resources | e-Seminars | About This Site

Short Courses Modular Courses

e-Learning Courses

ICH Good Clinical Practice E6 (R2)

RESULTS RETAKE

3% complete

Contents

1. Contents

DOWNLOAD MATERIALS:

This Course (PDF)
Your Certificate(PDF)

CONTENT NAVIGATION

1. Contents
2. Course Objectives
3. What is Good Clinical Practic
    1. What is Good Clinical

THE GLOBAL HEALTH NETWORK

Enabling research by sharing knowledge

Hereby Certifies that

YIN THET NU OO

has completed the e-learning course

ICH GOOD CLINICAL PRACTICE E6 (R2)

with a score of

94%

on

07/05/2018

This e-learning course has been formally recognised for its quality and content by the following organisations and institutions

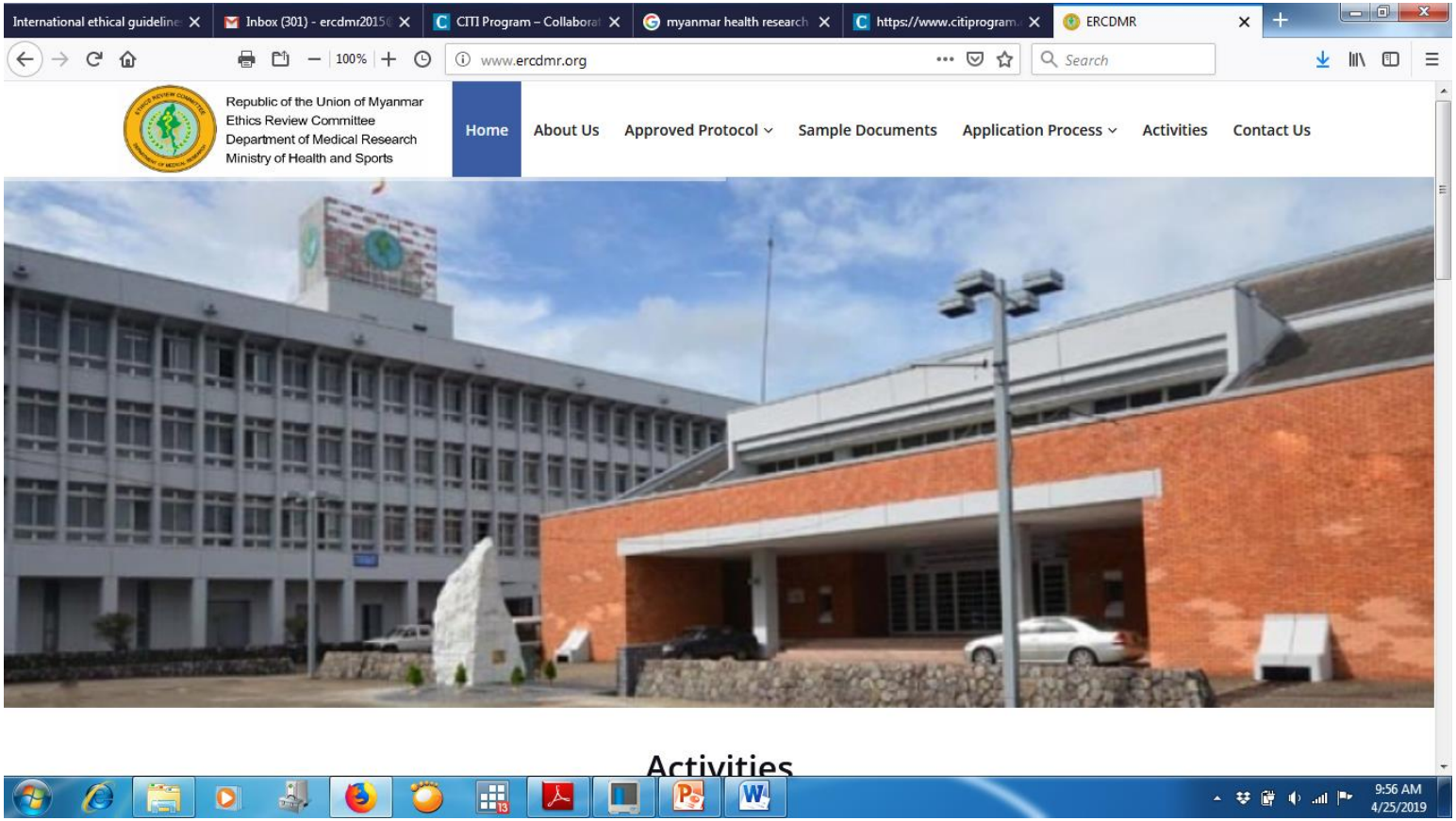
THE GLOBAL HEALTH NETWORK · WWARN · LSTM

*This ICH E6 GCP Investigator Site Training meets the Minimum Criteria for ICH GCP Investigator Site Personnel Training identified by **TransCelerate BioPharma** as necessary to enable mutual recognition of GCP training among trial sponsors.*

Global Health Training Centre
globalhealthtrainingcentre.org/elearning

Certificate Number 400572

www.irbdmr.gov.mm



- Facebook page- Myanmar Health Research Ethics Initiative

Guideline for submission to
Ethics Review Committee

Department of Medical Research
(DMR)
Ministry of Health
Republic of the Union of Myanmar

January 2016

The Government of the Republic of the Union of Myanmar
Ministry of Health and Sports
Department of Medical Research

ERC Number
Approval Number
Date of Approval
Project Title
Principal Investigator

Documents Accepted

The Ethics Review Committee on Medical Research Involving Human Subjects, Department of Medical Research, Ministry of Health and Sports approves to conduct the proposed research project as it is in full compliance with the Declaration of Helsinki, Council for International Organizations of Medical Sciences guidelines and International Conference on Harmonization in Good Clinical Practice guidelines.

Prof. Ko Thet Khin
Chairperson
Ethics Review Committee
Department of Medical Research

Thank You