System analysis and design for clinical trial control in Thailand

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การวิเคราะห์และการออกแบบระบบการกำกับดูแลการวิจัยทางคลินิกในประเทศไทย

นางสาวจารุณี กฤษณพันธ์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต

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จารุณี กฤษณพันธ์: การวิเคราะห์และการออกแบบระบบการกำกับดูแลการวิจัยทางคลินิกในประเทศไทย (SYSTEM ANALYSIS AND DESIGN FOR CLINICAL TRIAL CONTROL IN THAILAND). อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.ภญ.ดร.รุ่งเพ็ชร สกุลบำรุงศิลป์, 119 หน้า.

การศึกษาวิจัยนี้มีวัตถุประสงค์เพื่อศึกษาสถานการณ์ปัจจุบันของระบบการกำกับดูแลการวิจัยทางคลินิกในประเทศไทย ออกแบบระบบการกำกับดูแลการวิจัยทางคลินิก วิเคราะห์ส่วนขาดระหว่างระบบปัจจุบันและระบบที่เสนอ และพัฒนากลยุทธ์ เพื่อนำไปสู่การพัฒนาระบบการกำกับดูแลยาวิจัยทางคลินิก โดยการดำเนินการเป็น 4 ระยะ คือ ระยะแรกเป็นทบทวนวรรณกรรม ข้อมูลที่เกี่ยวข้องเพื่อเป็นข้อมูลในการจัดทำแบบสอบถาม ระยะที่สองเป็นการเก็บข้อมูลโดยใช้แบบสอบถามส่งทางไปรษณีย์ให้ผู้ที่เกี่ยวข้องกับการศึกษาวิจัยทางคลินิก ได้แก่ผู้รับอนุญาตนำหรือสั่งยาเข้ามาในราชอาณาจักรที่ยื่นขออนุญาตนำเข้ายาเพื่อการวิจัยทางคลินิก กลุ่มแพทย์ผู้วิจัย กลุ่มคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน กลุ่มเจ้าหน้าที่สำนักยา สำนักงานคณะกรรมการอาหารและยาที่เกี่ยวข้อง จำนวน 1260 คน มีผู้ตอบแบบสอบถามคิดเป็นจำนวนร้อยละ 26.9 ผลการศึกษาแสดงว่าผู้ที่เกี่ยวข้องมีความเห็นว่าระบบกำกับดูแลยาวิจัยทางคลินิกในปัจจุบันมีความเหมาะสมปานกลาง และเห็นด้วยกับการปรับปรุงให้เป็นไปตามระบบใหม่เพื่อให้มีความเหมาะสมมากขึ้น ระยะที่สามเป็นการวิเคราะห์ข้อมูลเพื่อหาความแตกต่างของระบบปัจจุบันและระบบที่เสนอใหม่ และการสัมภาษณ์เชิงลึกจากผู้แทนจากกลุ่มที่เกี่ยวข้อง เพื่อให้ได้แนวทางในพัฒนาและปรับปรุงระบบปัจจุบัน ซึ่งผู้วิจัยได้นำมาสังเคราะห์และพัฒนาเป็นกลยุทธ์ และ กลวิธี ในการพัฒนาระบบการกำกับดูแลการวิจัยทางคลินิก และในการศึกษาระยะที่ 4 ได้สอบถามความเห็นของผู้ที่เกี่ยวข้องต่อกลยุทธ์ กลวิธี และตัวชี้วัดโดยการเก็บข้อมูลจากแบบสอบถามที่แจกให้ผู้ที่เกี่ยวข้องในการประชุมประจำปี มีผู้ตอบแบบสอบถามคิดเป็นจำนวนร้อยละ 32.5 ผลการศึกษาพบว่าความเห็นเป็นเอกฉันท์ต่อการปรับปรุง พัฒนาการกำกับดูแลยาวิจัยทางคลินิกเพื่อให้มีการกำกับดูแลคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนของประเทศไทยที่มีมาตรฐาน ให้การกำกับดูแลยาวิจัยทางคลินิกของสำนักงานคณะกรรมการอาหารและยามีประสิทธิภาพ และให้มีการพัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้องในการสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย โดยกลยุทธ์ที่มีความสำคัญเร่งด่วนที่ควรนำไปสู่การปฏิบัติได้แก่ มาตรฐานของคณะกรรมการพิจารณาจริยธรรมการวิจัยและการรับรองหรือยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน ทั้งนี้การออกพระราชบัญญัติการวิจัยในมนุษย์ซึ่งอยู่ในระหว่างดำเนินการนั้นต้องอาศัยความสนับสนุนจากฝ่ายบริหารและการเมืองเป็นอย่างมาก ในระหว่างนี้สำนักงานคณะกรรมการอาหารและยาควรเป็นผู้ดำเนินการออกเกณฑ์ในการพิจารณายอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนที่พิจารณาโครงการที่ใช้ยาวิจัย กลยุทธ์อีกด้านที่สำคัญเร่งด่วนควรดำเนินการได้แก่ การกำกับดูแลยาวิจัยทางคลินิกของสำนักงานคณะกรรมการอาหารและยาให้มีประสิทธิภาพ ถึงแม้ว่าได้มีการออกระเบียบ กฎเกณฑ์ต่างๆที่เกี่ยวข้องกับยาวิจัยออกมาตั้งแต่ปีพ.ศ. 2532 ผลการศึกษาแสดงให้เห็นว่ายังมีความเข้าใจที่ไม่ถูกต้องและไม่ได้ดำเนินการตามระเบียบที่เกี่ยวข้อง ดังนั้นสำนักงานคณะกรรมการอาหารและยาควรเผยแพร่บทบาทหน้าที่ ระเบียบ กฎเกณฑ์ ขั้นตอนการดำเนินการที่เกี่ยวข้องกับการวิจัยทางคลินิกให้สาธารณชนและบุคคลที่เกี่ยวข้องทราบ ทั้งนี้การพัฒนาศักยภาพเป็นความสำคัญเร่งด่วนหนึ่งที่ต้องดำเนินการด้วยเพื่อให้ประเทศไทยสามารถวิจัยและพัฒนายาที่มีต้นกำเนิดในประเทศไทยได้ โดยอาจเริ่มพัฒนาศักยภาพโดยเรียนรู้จากการเข้าร่วมศึกษาวิจัยทางคลินิกที่มาจากต่างประเทศ ทั้งนี้กลวิธีเพื่อให้บรรลุวัตถุประสงค์และกลยุทธ์ต่างๆเป็นที่ยอมรับจากผู้เกี่ยวข้องที่ให้ความเห็นในการวิจัยนี้ ผลจากการศึกษาวิจัยนี้สามารถใช้เป็นข้อมูลพื้นฐานในการพัฒนานโยบายในการกำกับดูแลยาวิจัยทางคลินิกในประเทศไทย กำหนดกลยุทธ์และปรับปรุงการดำเนินการเพื่อพัฒนาประสิทธิภาพให้ดียิ่งขึ้นเพื่อให้เป็นมาตรฐานสากลและประชาชนมั่นใจว่าได้รับการคุ้มครองสิทธิและความปลอดภัยในการเข้าร่วมการศึกษาวิจัยทางคลินิก

ภาควิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่อนิสิต .....

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The purposes of this research were to analyze the current situation of the clinical trial system in Thailand, to design the practical clinical trial control system in Thailand, to identify the gap between current situation and expected clinical trial control system and to develop strategies for the clinical trial control system. This study consisted of four phases. The first phase was a literature review. Second phase used survey questionnaires asking current situation and opinion on the expected system mailed to 1,260 stakeholders including drug producers or importers, investigators, ethical committee's members and Food and Drug Administration personnel. The overall response rate was 26.9 percent. The results showed that even all parties considered that the current situation functioned moderately well, the proposed key issues in the designed model would create a better system. The third phase provided gap analysis and information from the in-depth interview with key informants from the parties to use in developing strategies to bring the current system upward to the designed model. Lastly, questionnaires were distributed to parties at their annual meeting to verify the proposed strategies with the response rate of 32.5 percent. The study showed that all parties are totally agree that the objectives of the clinical control system should focus on the standard and oversight of ethical committee, the effective control of investigational drug by Food and Drug Administration and capacity building in all related agencies. The current priority was the standard and accreditation of ethical committee, which needed political commitment to issue human research act. As the acts is still in-process, Food and Drug Administration should take initiation in establishing the recognition criteria for ethical committee in reviewing clinical trial of investigational drugs. Another priority was to improve efficiency of Food and Drug Administration's work. Even many regulations had been established, there were evidences showing lack of understanding and compliance. Therefore, Food and Drug Administration should promote understanding of role, regulation, procedure, and timeline to the public and concern parties. Lastly, capacity building was essential for conducting research and development especially for drugs originated in Thailand. It could start with capacity building for conducting clinical trial originated from foreign countries. Methods for development were proposed and agreed by concerned parties.

The result from this research could be the inputs for policy development and procedural improvement to strengthen the clinical trial control system in Thailand to be at the international standard and acceptance.

Department: Social and Administrative Pharmacy Student's Signature .....
Field of Study: Social and Administrative Pharmacy Advisor's Signature .....
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CONTENTS

Page

Page

Page

Page

Page

TABLES Page

TABLES Page

FIGURES

Page

ABBREVIATIONS

CRO	Contract Research Organization
EC	Ethical committee
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
MedResNet	Medical Research Network of the Consortium of Thai medical schools
SOP	Standard Operating Procedure
ThaiTECT	Thailand Towards Excellence in Clinical Trials

Chapter I

Introduction

1. Rational and framework.

Clinical Research is a part of research and development of drug product. Clinical research is a study of which healthy people or patients are involved. The objective of the clinical research is to assure that drugs are safe and effective. The clinical research consists of 4 phases. Each clinical trial phase has a different purpose. Clinical trial phase I is to test an experimental drug in a small group of healthy people (20-80) to evaluate drug's safety and determine a safe range of dosage and identify side effects. Clinical trial Phase II is to evaluate its effective and safety in a larger group of patients (100-300). Clinical trial phase III is to confirm its efficacy, safety, side effect in the large group of patients (1000-3000). Clinical trial phase IV is the post-marketing studies of which purpose is to collect more information such as risks, benefit, pharmacoeconomics and etc. These studies are pivotal for new drug research and development. During these processes, the risk of drug must have been closely monitored.

Since the safety of drug is scarcely know, especially at the early stage of development, subjects participated in the clinical trial must be carefully protected from the risk. There are many measures starting from well designed clinical trail, thoroughly scientific reviewed and complied with Good Clinical Practice (GCP).Even these drugs are approved to be marketed; they still need further studies of safety and effectiveness of use in the real situation due to during the research and development process, many factors are controlled in the form of inclusion or exclusion criteria such as age of the subjects, co-committed drug use, compliance and other factors. The magnitude of risk on safety will be reduced as information or knowledge on drug is more available.

In the past, there were only a few clinical trial researches in Thailand. Most of them were phase III or phase IV of clinical trial. The number of clinical trial is increasing in recent years. The number of investigational new drug importation' application is 101 in B.E. 2544 where as is 332 in B.E.2552, approximately 3 times with

in 8 years. They cover phase II through phase IV. Early phase such as phase II or Phase II/III is becoming more conducted in Thailand recently. Hence Thai subjects are likely to expose more to the risk by participated in early phase of clinical trial.

The increasing number of clinical trial in Thailand may be the result of many factors, which have been improved over the years. Hospitals have a good management and are equipped with new, high technology diagnose/treatment machines. Health care personnel are high qualification and well trained. More Ethical committees are established in compliance with the International Standard. In addition, a few institutions are becoming interested in conducting phase I clinical trial, which is the first time of drug use in human.

This is very crucial for early phase of clinical trial to ensure that the safety has adequately been reviewed and the right and safety of participants in the research are protected. There is no specific law or regulation concerned about human right or patient right participating in clinical trial research. Therefore, the right may be not adequately protected.

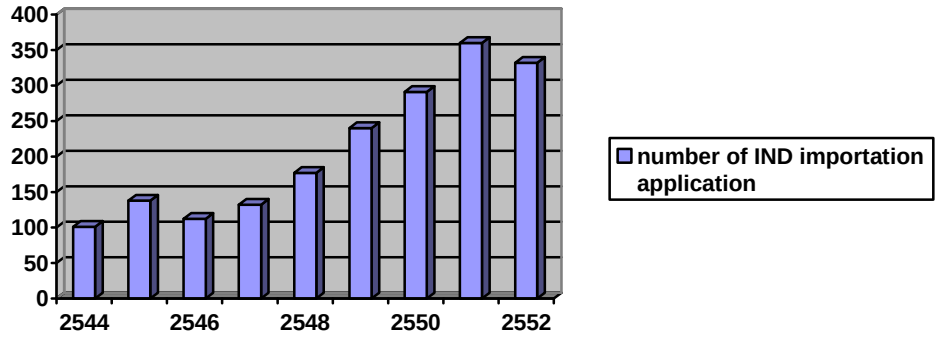

Figure1: The number of Investigational New Drug's importation application during B.E.2544-2552 (Bureau of Drug Control, Food and Drug Administration)

Recent years, there are more clinical studies on Bioequivalence in Thailand due to the Food and Drug Administration regulation that new generic drug must submit bioequivalence study to assure that the quality and safety is equivalent to new drug already registered. These studies must be conducted in Thai. However, 37 study reports

are not accepted by Food and Drug Administration during B.E 2550-2553. The causes of rejection could be classified into 2 categories which are non-compliance with Good Clinical Practice (GCP) and non-compliance with scientific guideline such as Bioanalytical Method Validation and ASEAN Guideline for the conduct of Bioavailability and Bioequivalence Study. The rejection of these studies causes loss not only to the sponsor that provide money support but also to the subject participated in the study. They scarify themselves for the benefit of study but the study failed. This can be considered that the right of subject is not adequately protected.

Good Clinical Practice (GCP) could be considered as basic principle for protecting subject. However, Complying with GCP is a voluntary measure in Thailand. There is no responsible agency or regulation on GCP.

Even there are many measures to minimize the risk and increase the protection of subject participating in clinical trial, there are no regulatory or legal framework to implement those measures. Therefore government should provide the legal framework for clinical trials. The aim should be to protect the safety and rights of the subjects participating in a trial, and to ensure that trials are adequately designed to meet scientifically sound objectives. These aims may be met by several means, including the specification of the investigator's qualification, requirement for review and approval of the protocol by relevant scientific and/or ethics committee and mandatory GCP compliance.

Even though Food and Drug Administration is the national agency which permits the importation of investigational drugs or test drugs for clinical trial research in Thailand, there is no agency or institution responsible for approval or control the clinical research. There is no study or review of opinion of people or other stakeholders on clinical trial in Thailand. Therefore, it is important to study the situation and perception of stakeholders on Clinical Trial Research in Thailand. This information will be useful for formulating the policy proposal on clinical trial research management in Thailand. This study will analyze the gap between the standard process and the current situation in order to develop model for clinical trial control system in Thailand.

2. Objectives

1. To analyze the current situation of the clinical trial system in Thailand
2. To design the practical clinical trial control system for Thailand
3. To identify gaps between the designed clinical trial control system and Thai current system
4. To develop the strategies for the clinical trial control system

3. Scope of the study

The clinical trial study covers all studies in health-related interventions involved human. These interventions include drug, medical devices, medical procedures, behavioral treatments, preventive care, etc. This study focused only on the clinical trial using drug products.

4. Expected benefit

The Food and Drug Administration could use the result to strengthen the clinical trial control system in Thailand and to assure that the right of human subject is protected.

5. Conceptual framework of clinical trial control system

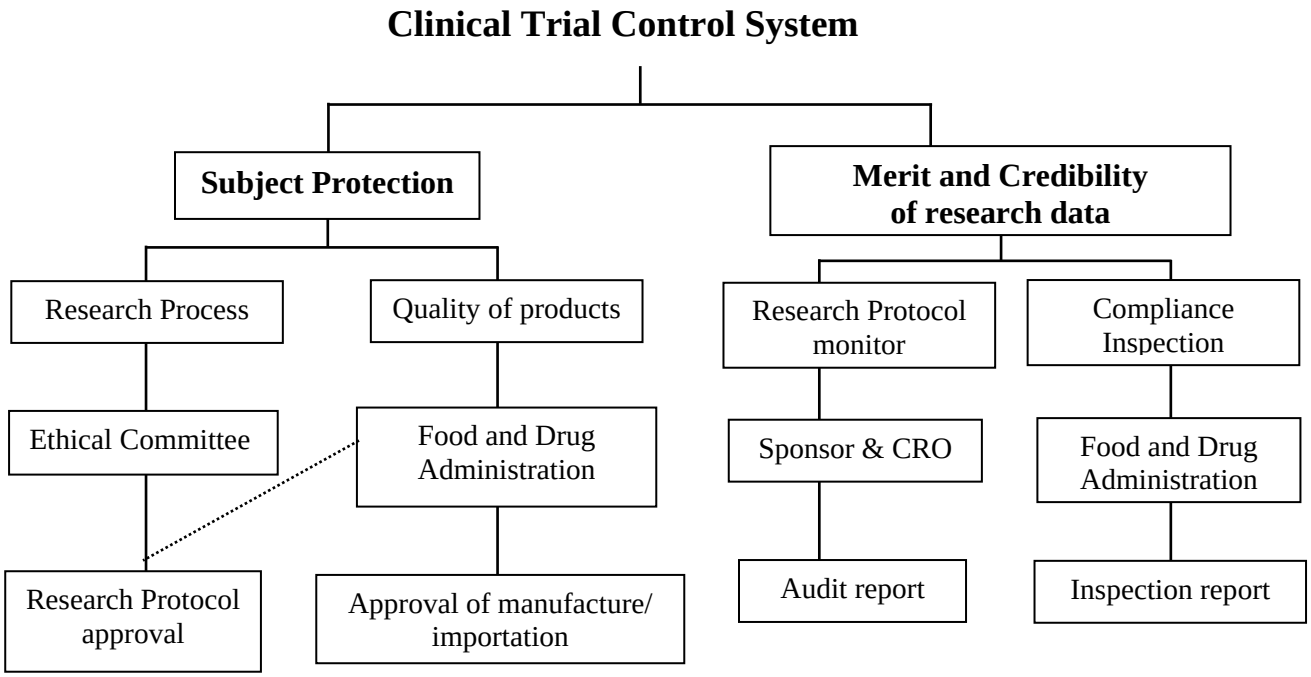

Figure 2: Conceptual Framework of Clinical Trial Control system

The objectives of the clinical trial control system are the subject protection and the merit and credibility of research data. There are many organizations and various measures to fulfill these objectives. The first priority is to assure that human subjects participating in clinical trial are protected from any harm. Two main aspects related to the subject protection are the quality of product used in the clinical trial and the process of conducting the clinical trial.

The quality of product is the main responsibility of Food and Drug Administration. Therefore, Food and Drug Administration reviews the documents related to the quality of the product. On the other hand, ethical committee is the main organization to ensure the ethical of conducting the clinical trial. Ethical committee reviews the clinical study protocol whether is rational, well scientific-designed and has a proper measure to detect, manage and prevent any adverse event may occur. In addition the approval of research protocol by Food and Drug Administration is an additional measure to assure that the subjects are protected and the drugs are used specifically only in the approved study protocol and the clinical site specified in protocol.

The merit and credibility of data obtained from clinical trial is assured by monitoring by sponsor, contract research organization, Food and Drug Administration and ethical committee. The monitoring is considered as a quality assurance process.

Chapter II

Literature review

1. Introduction to clinical trial

The definition of clinical trial by World Health Organization is any research study that prospectively assigns individual research participants, or groups of research participants, to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioral treatments, process-of-care changes, and preventive care. In other words particularly for pharmaceutical, clinical trial means an investigation in respect of a drug use in humans that involves human subject and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug or ascertain the safety or efficacy of the drug. (Health Canada). Clinical research is a study of which healthy people or patients are involved. The clinical research consists of 4 phases. These studies are pivotal for new drug research and development. Even these drugs are approved to be marketed; they still need further studies of safety and efficacy of use in the real situation due to many factors are controlled in the form of inclusion or exclusion criteria such as age of the subject, co-committed drug use, etc and compliance during the research and development process.

As a government agency, the regulatory framework of clinical trial is needed in order to

-protect subject or volunteer who participate in clinical trial especially on safety issues

-ensure the merit of scientific research that the study has been well designed and considered all aspects of safety and ethical issues

-ensure the credibility of data that will be used in the marketing authorization evaluation.

Even though it is well recognized the need of regulatory framework on clinical trial, not all countries has implemented or fully implemented. This is due to many causes

such as political will, legislation environment and resources. The main role and responsibility of Thai Food and Drug Administration, a government agency, is to protect consumer's health especially to ensure safety, quality and efficacy of drug by pre- and post-marketing measures. This responsibility does not exclude drug that is not authorized to market in the country. Food and Drug Administration's responsibility to control and assure users getting no harm covers all drug uses.

1.1 Clinical trial Process

There are many process involved in clinical trial as following:

1. Protocol development.

Sponsor or investigator will develop clinical protocol in order to find the information for specific purpose.

2. Ethical committee review

The protocol and related documents such as inform consent, patient information will be submitted to Independent Ethical Committee or Institutional review board for ethical consideration.

3. Clinical trial authorization application to Drug regulatory authority

Sponsor or investigator will submit the Clinical Trial authorization application to Drug regulatory authority.

4. Clinical trial protocol review by Drug regulatory authority

The protocol and related documents including Chemical and Manufacturing control (CMC) will be review by Drug regulatory authority.

5.Clinical trial authorization and monitoring

The clinical trial authorization will issue to the applicant. The protocol could be conducted. Monitoring of conducting will be done by Ethical committee and Drug regulatory at the before, during and after the trial conducted.

6.Protocol amendment

During the conducting of trial, protocol could be amended for changes such as new site for trial, new information related to safety issues. Regulatory bodies such as Ethical committee and Drug regulatory authority should be informed these changes.

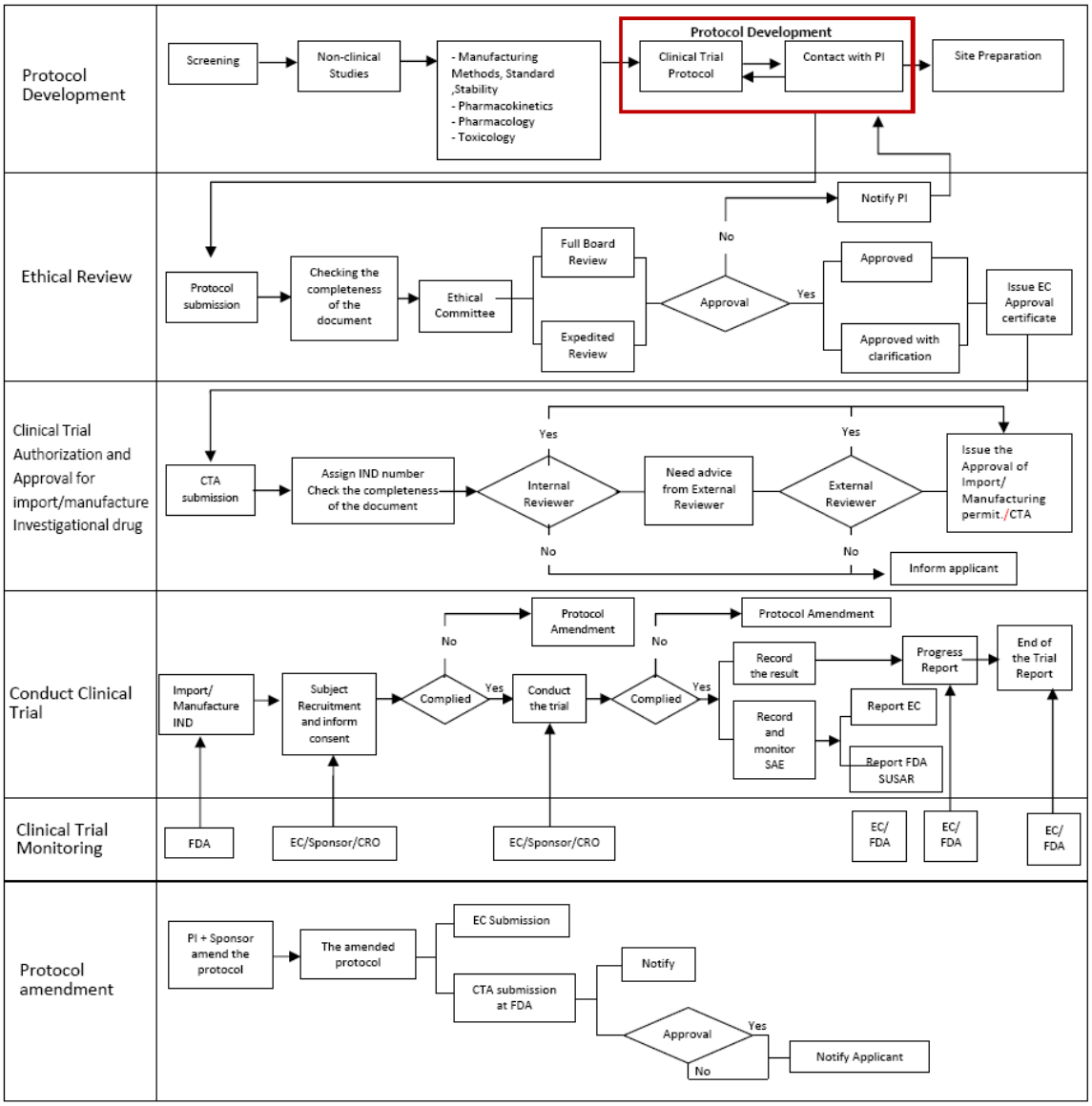

Figure 3: The diagram of process related to clinical trial

2. Clinical trial control system in other countries

Clinical trial control system is available and implemented in many countries both developed and developing countries. The experiences from other countries are selected and presented in this study. Canada's clinical trial control system is an example for clinical trial control in developed country. Singapore's clinical trial control system is an example for developed country in ASEAN region. The details are as follow:

2.1. Clinical trial Control System in Singapore

2.1.1.Responsible agency

Health Science Authority (HSA) is a Drug Regulatory Authority in Singapore who is responsible for regulating drugs, innovative therapeutics, medical devices and health-related products. HSA is divided into 3 main groups, which are Heath Products Regulation Group, Blood Services Group and Applied Sciences Services Group. The Health Products Regulation Group (HPRG) ensures that drugs, innovative therapeutics, medical devices and health-related products in Singapore are regulated to meet appropriate standards of safety, quality and efficacy.

2.1.2. Legislation

The Medicine Act 1975 and the Medicines (Clinical Trials) (Amendment) Regulation 1998 are the legal basis to regulate the clinical trial in Singapore. HSA has been empowered to oversight the clinical trial by Chapter 176, Sec 18 and 74 of the Medicines Acts. All clinical trials in Singapore require the approval from Clinical Trial Branch, Health Products Regulation Groups, HSA before conducted.

2.1.3. Procedure

Sponsor is the responsible person to apply for clinical trial approval with the HSA, however HSA will issue the approval to the principal investigator, which is specific for each study protocol, each institution or each site involved in the study. The clinical trial approval is in the form of a Clinical Trial Certificate (CTC). If the clinical trial materials will be imported, the sponsor has to request the Clinical Trial Materials (CTM) import permit from HSA. This could be submitted concurrently with application for Clinical Trial Certificate (CTC). However, HSA will issue the Clinical Trial Materials imported permit to the sponsor who will actually import the materials and then distribute to the investigator.

HSA will approve the clinical trial with the advice from the Medical Clinical Research Committee (MCRC). This committee has been established to review and

oversee the conduct of clinical trial. The role and responsibility of this committee is to review and deliberate on new applications for clinical trial certificates, amendments to clinical trial protocols and informed consent documents, serious adverse event reports and request for clinical trial certificate extension.

The information, which is needed to be filled in the clinical trial application as follow;

1.Trial Information

2.Study Drugs to be investigated

3.Comparator Drugs to be used (if applicable)

4.Concomitant Products to be used (if applicable)

5. Local Trial Centers, Principal Investigator(s) and IRB Details

7.Sponsor (Local Contract Research Organization and Overseas)

8.Supporting documents such as

-Clinical Trial Protocol

-Patient Information Sheet and Informed Consent form

-Subject Recruitment Procedures and Advertisements (if applicable)

-Listing of Overseas Trial centers (if applicable)

-Principal Investigator(s) Curriculum Vitae

-GMP Certificate(s) or Certificate of Accreditation

-Certificate of Analysis (CoA) (if applicable)

-Letter of approval issues by Institutional Review Board

Since January 2006, parallel submission to HSA and the respective Institutional Review board are permitted. The regulatory approval would be issued independent to the ethics approval. The clinical trial could be conducted only when both regulatory and ethic approved. In addition, sponsor has to submit the copy of ethical approval to HSA.

2.2.Clinical Trial Control System in Canada

2.2.1. Responsible agency

Health Canada is a Federal department, which is engaged in various activities related to health. There are many Directorate in Health Canada. The relevant Directorates involved

in pharmaceutical products including biological products are Therapeutic Products Directorate and Biological and Genetic Therapies Directorate. For the clinical trial on pharmaceutical product, Office of Clinical Trials, Therapeutic Product Directorate is the responsible office who will review and authorize the clinical trail to be conducted in Canada. Regulatory Affairs Division, Biologics and Genetic Therapies Directorate is the responsible office who will review and authorize the clinical trial on biological products to be conducted in Canada.

2.2.2. Legislation

There has been a regulation on drug used for the purpose of clinical trial since early 1960 under the Food and Drug act. The recent amendment or regulation concerning clinical trial control is Part C, Division 5 of the Food and Drug Regulation, 2001.

The main framework of this regulation is the authorization requirement for Phase I, II, III clinical trail and marketed drug whose propose used would not be the same as authorized condition of use when approved. In addition, there are clearly stated of requirement on document, labeling, record keeping, report of serious unexpected adverse drug reaction. Sponsor's obligation is also clearly stated in the regulation including Good Clinical Practices (GCP). Even though the clinical protocol is authorized by Health Canada, the conduct of trial could not be done before receiving the approval of a research ethics board.

2.2.3. Procedure

Sponsor is the responsible person to apply for clinical trial approval or authorization. The Clinical Trial Application (CTA) has to be submitted to responsible office in Health Canada before initiate clinical trial. Responsible office will review and notify the result to sponsor within 30 days except for some categories such as bioequivalence within 7 days. The requirement for clinical trail authorization has been clearly identified in the regulation such as protocol, clinical trial attestation etc. Guidance for Clinical Trial Sponsors is also available to help sponsor in preparation and filing the Clinical Trial Application. The format of application is adopted from ICH as CTD format in order to facilitate and familiarize the sponsor and reviewer from development to

marketing authorization. The detailed or complexity of data may be different from stage of development but the main components still remain. CTA requirement consists of 3 modules which are;

Module 1: Administrative/Clinical Information

Module 2: Common Technical Document Summaries

Module 3: Quality

The Administrative/clinical information in Module 1 should include investigator's brochure, protocol synopsis, informed consent, clinical site information, Canadian Research Ethics Board(s) refusal (if any), Foreign refusals (if any), letter of access (to allow Health Canada to access related master files) etc.

In summary, the regulatory framework could be divided into two main functions which are pre-, and during conducting clinical trial.

Regulatory framework on pre-conducting clinical trial consists of two steps. The first step is the authorization or certification to conduct the trial. This step is to approve the clinical protocol based on scientific review. The second step is the approval of product importation or manufacture. In Singapore, there are both steps and could be submitted at the same time. In Canada, there is only one step for clinical trial authorization however this could be use for importation and distribution in Canada.

Clinical Trial regulation on conducting the trial or the oversight of Clinical trial, there are two components which is Good Clinical Practices (GCP) inspection, and IRB/IEC During the conducting the trial, Canada and Singapore have an oversight of clinical trial by GCP inspection.

2.3.The current clinical trial control system in Thailand

2.3.1. Responsible agency

Food and Drug Administration, Ministry of Public Health is a government agency whose main role and responsible is to protect consumer's health especially to ensure safety, quality and efficacy of health products. Drug Control division is responsible for the drug products including pharmaceuticals and biological products. In 2001 Drug control division established a new unit to be responsible for clinical trial. At present,

Investigational New Drug unit, Pre-marketing division, Bureau of Drug Control is the responsible unit for clinical trial related issues.

2.3.2. Legislation

According to Drug Act B.E.2510 and amendment, all drugs must be registered before production, importation and sell in Thailand as mention in Section 12 and Section 79, the detailed as follows:

Section 12: No person shall produce or sell a modern drug, or import or order a modern drug into the kingdom, unless he/she has obtained a license from the licensing authority

Section 79: Any person licensed to produce or import drugs, who wish to produce or import drug is required first to the competent officer for registration of the formula. Upon receipt of a certificate of formula registration, the drug may be produced or imported. However, some drugs could be exempt from registration as mentioned in Section 79 bis as follows:

Section 79 bis: Section 79 shall not be applied to

(1) Drugs that is pharmaceutical chemicals or semi-processed pharmaceutical chemicals that is not packaged drugs,

(2) Herbal drug

(3) Sample drugs that are received permission to produce, import into the Kingdom for application to register in accordance with the rules, regulation and conditions prescribed in Ministerial regulation

(4) Drug that is permitted to import into the Kingdom in accordance with the rules, procedures and conditions prescribed in the Ministerial Notification.

Refer to Section 79 bis (4), Ministerial Notification no.14: Requirement, process and conditions for importing drug into Thailand with exemption from product licensing is issued in B.E.2532. This exemption is only for the purpose of clinical trial/study, analysis, exhibition or donation.

2.3.3. Procedure

Applicants must be either holders of Drug Import License, Thai Red Cross, Government Pharmaceutical Organization, or Ministry/Department responsible for

prevention and treatment of diseases**.** The application with relevant document should be submitted at Bureau of Drug control, Food and Drug Administration. The required documents are as follow;

-Labels of every package size

-Package Insert

-Investigator's Brochure

-Patient Information Sheet

-Summary of Clinical Trial Protocol (Thai)

-Clinical Trial Protocol

-Chemical, manufacturing and control documents

-Ethical approval from FDA recognized Institutional Review Board: IRB or Independent Ethic Committee: IEC

After reviewing the documents, Food and Drug administration will permit to import drug or clinical material into Thailand and conduct the study.

Most of universities which have faculty involve in clinical trial have their Institutional Review Board (IRB) but there is no authorities or law and regulation to control and monitor Institutional Review Board (IRB)/Independent Ethical Committee(IEC) and their function. Currently, FDA accept Ethical Committee (EC) approval certificate of the trials conducted under ten institutions which are;

1. Ministry of Public Health
2. Faculty of Medicines, Chulalongkorn Univesity.
3. Faculty of Medicines, Siriraj Hospital
4. Faculty of Medicines, Ramathibodi Hospital
5. Faulty of Tropical Med, Mahidol University
6. Faculty of Medicines, Chiangmai University.
7. Faculty of Medicines, Khonkan University.
8. Faculty of Medicines, Prince Songkhalnakarin University.
9. The Royal Thai Army Medicine Department.
10. Institute for the development of Human Research Protection (IHRP)

Table 1: Comparison of Component in Clinical Trial Control system in three countries:

	Singapore	Canada	Thailand
Responsible organization	Clinical Trial Branch, Health Products Regulation Groups, HSA	-Office of Clinical Trials, Therapuetic Product Directorate, Health Canada (For Pharmaceuicals) -Regulatory Affairs Division, Biologics and Genetic Therapies Directorate, Health Canada (For Biological products)	Investigational new Drug unit, Pre-marketing division, Bureau of Drug Control, Food and Drug Administration
Legislation	-The Medicine Act 1975 and the Medicines (Clinical Trials) (Amendment) Regulation 1998 -Chapter 176, Sec 18 and 74 of the Medicines Acts	-Food and Drug Act -Part C, Division 5 of the Food and Drug Regulation, 2001	Refer to Section 79 bis(4) of Drug Acts, Ministerial Notification no.14: Requirement, process and conditions for importing drug into Thailand with exemption from product licensing is issued in B.E.2532. and amendment B.E. 2552

	Singapore	Canada	Thailand
Procedure	-Clinical Trial Certificate (CTC) -Clinical Trial Materials (CTM) import permit	Clinical Trial Application (CTA)	Import permit for Clinical trial materials.
	Parallel submission of CTC and EC approval	No EC approval required during CTA authorization but Clinical trial could be conducted only when EC approved.	EC approval required during review for permission except that drug has a certificate of free sale from Country of Origin or certificate of pharmaceutical product.

In summary, there were two similar aspects in all three countries. First, there were specified unit responsible for clinical trial control. Second, there was a procedure to approve the use of drug in clinical trial with differences in the detailed. There were two steps which were clinical trial certificate (CTC) and clinical trial materials import permit (CTM) in Singapore. Only one step, clinical trial application (CTA) was implemented in Canada. There was only one step, import permit of clinical trial materials in Thailand.

Differences in requirement of ethical committee approval certificate during the approval of the use of drug in clinical trial were prominent among three countries. These ranged from no requirement in Canada, requirement before approval and requirement before submission application.

As regulatory requirement for clinical trial has been implemented in many countries, differences among countries exist. Industry faces a difficulty in developing drugs for global market. In addition, cost of drug research and development increased dramatically as well as the increasing expectation from the public to access the new drug without unnecessary delay. Therefore, there is a need for harmonization. International

Conference Harmonization (ICH) has been established since 1990 with the cooperation between regulatory agencies and industry association from three regions which are Europe, Japan and US. These three regions are the drug research base countries. Over the years many ICH Harmonized Tripartite guidelines have been developed. These guidelines could be divided into Safety, Quality and Efficacy. The guideline which is directly related to clinical trial is Guideline for Good Clinical Practice (E6). Good Clinical Practice (GCP) is an ethical and scientific standard for designing, conducting, recording and reporting clinical trial involved human subjects. This guideline provides a harmonized standard to facilitate the acceptance of clinical data to the regulatory agency within three regions.

The content of Guideline for Good Clinical Practice covers areas which may effect the conduct and reliable of clinical trial. The principle of ICH GCP has been laid out. Role and responsibility of stakeholders such as institutional review board/ independent ethics committee, investigator, sponsor are stated. Essential documents for clinical trial starting from before, during and after conducting clinical trial have been identified.

Good Clinical Practice (GCP) has been formally announced by the cooperation between Ministry of Public Health and Ministry of University Affair (currently changed to, Ministry of Education) in 2000. However, this is a voluntary measure. There is no law or regulation to control, monitor or oversight the clinical trial. As this ICH GCP is an international guideline and well recognized, it could be used as a bench mark to develop a required clinical trial control system in Thailand.

However, there is no particular section related to regulatory agency. Therefore there is a need to find additional bench mark document to define desired regulatory agency role and responsibility. World Health Organization (WHO) is an international organization who direct and coordinate authority for health within the United Nations. WHO's responsibility covers from providing leadership on global health, evidence-based policy option, providing technical support to countries and monitoring and assessing health trends and setting norms and standards. WHO has developed an assessment tool to serve as a benchmark and to monitor progress of national regulatory authorities for vaccine. This assessment tool consists of indicators for regulatory functions, which are

marketing authorization and licensing, post-marketing surveillance including adverse events following immunization, lot release, laboratory access, regulatory inspections of manufacturing sites and distribution channels and authorization and monitoring of clinical trials. These indicators could also be applied for regulatory authority for pharmaceuticals product. For the function of authorization and monitoring of clinical trials, there are 6 indicators as following; system for regulatory oversight of clinical trials, quality management system for oversight of clinical trial, human resource management, format and content for submission of clinical trials application, scientific review of clinical trials application, assurance of ethical oversight. These indicators could be used as a benchmark for developing a required clinical trial control system in Thailand in addition to ICH GCP in order to cover the whole system of clinical trial control.

Chapter III
Methodology

The study consisted of four study objectives, which were acquired in order. This study was divided into three phases in order to serve four objectives of the study sequentially. Each phase would employ different method, study sample and data collection.

The four objectives of this study were;

Objective 1: To analyze the current situation of the clinical trial system in Thailand

Objective 2: To design the practical clinical trial control system for Thailand

Objective 3: To identify the gap between the current situation of clinical trial control system and the designed clinical trial control system

Objective 4: To develop strategies for getting the designed clinical trial control system.

Study design

This study was conducted in four phases in order to serve particular objectives of the study sequentially. Both qualitative and quantitative research methodologies were used. The study started with a literature review of the related documents for current situation of clinical trial in Thailand. The international guidelines and the assessment tool related to the clinical trial were also reviewed. Next step was to develop the questionnaire, which was used as a model to analyze the opinion of the stakeholders on the current situation and the designed situation. This first questionnaire was developed based on the result from literature review. The result from this first questionnaire was analyzed to find out the gaps or the differences between the current and the designed situation which was the third objective of this study. Then the In-depth Interviews were conducted in order to get information for developing the strategies to improve and strengthen the clinical trial control system. Lastly, the second questionnaire was developed to analyze the opinion of the stakeholders on the proposed strategies. The result was analyzed and the policy

recommendation for getting the designed clinical trial control in Thailand was proposed. The summary of study process is presented below:

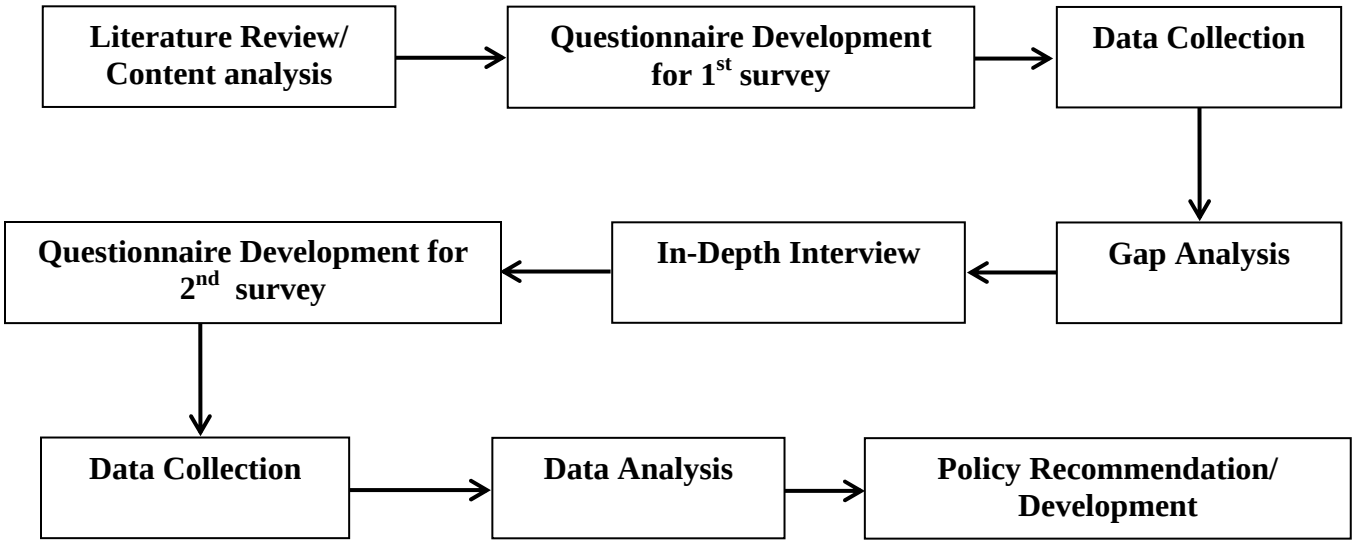

Figure 4: Diagram of study process

1. **Objective 1: To analyze the current situation of the clinical trial system in Thailand**
   Objective 2: To design the practical clinical trial control system for Thailand

These two objectives were combined using one questionnaire survey. The related documents to the clinical trial in Thailand such as Drug Acts, Ministerial Notification, Food and Drug Administration regulation, statistics data of investigational drug's importation application including international standards and norms were reviewed. The key components in the Guideline on Good Clinical Practice developed by International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human use (ICH-GCP) and the World Health Organization's data assessment tool for Drug regulatory system for vaccine were used to develop the questionnaire. The questionnaire was to examine the experiences and opinions of the

respondents. The questions concerning the current situation used the likert scale to describe the respondent's opinion ranging from 1 as not appropriate to 5 as most appropriate. The question concerning the designed system for clinical control used the binary scale as agree and disagree.

1.1 Study sample

All stakeholders involving clinical trial in Thailand were included. The list of 30 licensed importers and 15 of the contract research organizations represented the sponsor group of the clinical trial. These sponsors were the sponsor who submitted the application for Investigational drug's importation for the clinical trial in 2011. There were numbers of ethical committees in Thailand. In addition they established the Forum for Ethical Review Committees in Thailand (FERCIT) in 2000. As only ten ethical committees in Thailand that Food and Drug Administration recognized, in order to collect the opinion from most ethical committee, the 756 members of the ethical committee members listed in FERCIT served as target population of the independent ethical committee or institutional review board group. The list of 454 investigators who had the history of participating in the clinical trials which used investigational drugs with the importation approval from Food and Drug Administration in Thailand were used as population for the investigator group. Five of the Food and Drug Administration personals who involved in Clinical trial served as the regulator group.

1.2 Mode of data collection

The questionnaires were sent by mail to the study samples for self-administration to survey the opinion on the current situation and the designed system. The multi-rater was used for the aspects of current situation because the respondents could have various opinions due to their experiences. This multi-rater feedback would provide the data from all points of view.

1.3 Questionnaire

The questionnaire consisted of three parts which were demographic data of the respondents, the opinion on current situation of clinical trial control system in Thailand

and the opinion on the designed clinical trial control system. The questionnaires were developed based on Guideline for Good Clinical Practice (ICH-GCP) and World Health Organization's assessment tools for regulatory authority.

The draft of questionnaire was tested with five people whether they understood and were able to answer the questionnaire. Then the questionnaire was amended and distributed to the study sample.

1.3.1 Demographic data

Many demographic data were collected in order to identify and compare the opinion among different stakeholders group. Role of the respondent in clinical trial as sponsor, investigator, ethical committee, contract research organization (CRO) and regulator (Food and Drug Administration personnel) were collected. The respondent's experience was collected as the number of years in the particular role. Education and training data were also collected. Some particular training programs, which were Ethical training, Good Clinical Practice (GCP) training, were asked.

1.3.2 Opinion on the current situation of clinical trial control

The survey on the current situation of clinical trial control consisted of four aspects which were the regulatory control aspects by Food and Drug Administration, the ethical control aspects by Ethical committee, the clinical trial registry aspects and the procedural aspects.

1.3.2.1 Regulatory control aspects by Food and Drug Administration

Clinical trial study is a study involving human subject in order to investigate pharmacokinetics, pharmacodynamics of the drug and any adverse events in respect of the drug as well as to ascertain the safety or efficacy of the drug. It covers the study of the drug that is already registered, is not registered and is under development process. Food and Drug Administration requires that not-registered drug used in clinical trial has to get the approval by Food and Drug Administration before conducting clinical trial. Whereas using registered drug in clinical trial is not required to get the approval from Food and Drug Administration before conducting clinical trial. It is a voluntary procedure for the sponsor or the investigator to ask for approval from Food and Drug Administration. Data

from the survey would represent the current situation of the clinical trial conducted in Thailand and the compliance with the regulations.

1.3.2.2 Ethical control aspects by Ethical committee

Before conducting any clinical trials, the approval from the ethical committee is required. The ethical committee in Thailand could be categorized as Independent Ethics Committee and Institutional Review Board. The question of whether and where the respondents submit for ethical approval or clearance would show the level of compliance with the ethical control aspects.

1.3.2.3 Clinical trial registry aspects

A clinical trial registry is a system for registering the clinical trial. The objective of the system is to strengthen the transparency of the clinical trial, to enhance the accountability of clinical data obtained and to facilitate the access of patient to new drug or new treatment by participating in the clinical trial. Mostly is an online-register. The question of whether the respondent registered the clinical trial with any clinical registries would represent the level of transparency and accessibility to information.

1.3.2.4 Procedural aspects

Fifteen questions related to procedural aspects with Food and Drug Administration and ethical committee were included in the questionnaires.

1.3.3 Opinion on the designed system of clinical trial control

The survey on the designed system of clinical trial control consisted of two aspects which were the proposed procedural and the appropriate organization for governing ethic’s law, clinical trial registry and GCP compliance.

2. Objective 3: To identify the gap of the current situation and the expected clinical trial control system

2.1 Mode of data collection

This phase emphasized on the data analysis of the differences between the current situation and the desired situation including the differences opinions on the designed clinical trial control system. The comparison of score obtained from all stakeholders group was analyzed including information from literature review.

3. Objective 4: To develop the strategies for the designed clinical trial control system

3.1 Mode of data collection

3.1.1 In-depth Interview

The In-depth Interviews were conducted to gain the detailed information that was beneficial for developing the strategies to bring the current system upward to the designed system. Four representatives from sponsor, investigator, CRO and FDA were interviewed. The main topics were their opinions on the current situation, the problems or obstacles, the desired system or environment and the suggestion to improve the current situation. Each interview took approximately two hours.

3.1.2 The second questionnaire

The second questionnaire, which was the questionnaire on the strategies for improving clinical trial control system in Thailand, was developed based on the collected information from the first survey and in-depth interview. The second questionnaire was distributed to all stakeholders who attended the ThaiTECT annual meeting. ThaiTECT was an abbreviation of Thailand Towards Excellence in Clinical trials. It was formed by several groups of people involved with clinical trials. The groups consisted of investigator, ethic committee, sponsor, contract research organization, medical research center and

Food and Drug Administration.

The questionnaire was to examine the opinions of the respondents on the objectives, strategies and method in order to have a good clinical trial control system in Thailand. The questions concerning the objectives and the strategies used binary scale as agree or not agree. In addition the opinions on the importance and the feasibility of each strategy were collected using the likert scale from 1 to 3 as less, medium and most important, and less, medium and most feasible accordingly. The priorities were then assigned based on scores obtaining from importance and feasibility. The indicators were included in the questionnaires and using the likert scale from 1-5 as inappropriate, less appropriate, appropriate, more appropriate and most appropriate accordingly.

3.2 Questionnaire

The questionnaire consisted of two parts, which were demographic data of the respondents and the opinion on the proposed strategies for the designed clinical trial control system

The draft of questionnaire was tested with three people whether they understood and were able to answer the questionnaire. Then the questionnaire was amended and distributed to the study sample.

3.2.1 Demographic data

Many demographic data were collected such as professional, role in clinical trial as sponsor, investigator, ethical committee, contract research organization (CRO) and regulator (Food and Drug Administration personnel). The respondent’s experience was collected as the number of years in the particular role.

3.2.2 Opinion on the proposed strategies for the designed clinical trial control system

The survey on the proposed strategies for the designed clinical trial control system consisted of four aspects which were the objectives of the designed clinical trial control system, the strategies for each objective, the method for each strategy and the indicators.

3.2.3 Aspects on the objectives of the designed clinical trial control

The proposed three objectives of clinical trial control system were to have a standard ethical committee, to have effectively clinical trial control by Food and Drug Administration and to strengthen capacity building in related agencies in order to promote the clinical trial in Thailand.

3.2.4 Aspects on the strategies for each objective

There were two proposed strategies for the first two objectives and four proposed strategies for the third objective, the detailed as follows:

Objective1: to have a standard ethical committee	Strategy 1: An accreditation or recognition system
	Strategy 2: National standard for Ethical committee
Objective 2: to have effectively clinical trial control by Food and Drug Administration	Strategy 1: Develop standard, procedure and criteria for evaluation
	Strategy 2: Develop safety monitoring process
Objective 3: to strengthen capacity building in related agencies in order to promote the clinical trial in Thailand	Strategy 1: Increase the number of qualified investigator
	Strategy 2: Develop database and network information related to clinical trial
	Strategy 3: Increase the number of clinical site with good quality.
	Strategy 4: Increase knowledge on research and development of drug or herbal drug

3.2.5 Aspects on the methods for each strategy

Each strategy had a various proposed methods to be implemented in order to fulfill the objectives. The detailed of methods were presented as follows:

Objective1: to have a standard ethical committee	
Strategy 1: An accreditation or recognition system	Method 1: Define or set up a specific agency responsible for accreditation or recognition
	Method 2: Monitor periodically every two years
Strategy 2: National standard for Ethical committee	Method 1: Each institution formally establishes an ethical committee or recognizes other institution's ethical committee complied with ICH-GCP standard
	Method 2: Food and Drug administration issues the regulation on ethical committee recognition
	Method 3: Thailand has Human Research Acts
Objective 2: to have effectively clinical trial control by Food and Drug Administration	
Strategy 1: Develop standard, procedure and criteria for evaluation	Method 1: Set up quality system including quality manual, SOP and criteria for evaluation
	Method 2: Issue the regulation that clearly identify types of investigational drug used clinical trial which are -drug never registered in any countries -drug already registered with new indication, new posology or new user group. -drug already registered (Phase IV)

	Method 3: Issue the regulation that clearly specifies role and responsibility of involved parties, approval, monitor and revoke process
	Method 4: Online submission for application
	Method 5: Report the finished or ending of clinical trial study within specific timeline
	Method 6: Report the progress of clinical trial study within specific timeline
	Method 7: Set up the consultation process for developing the clinical trial protocol
	Method 8: Improve the timeline for approval which are - 20 days for new protocol of pharmaceutical products - 60 days for new protocol of biological products - 5 days for already approved protocol.
	Method 9: Update the progress of clinical trial in Thailand clinical Trial Registry (TCTR).
	Method 10: Provide the registered number of TCTR in the application for manufacture or importation of drug for clinical trial
Strategy 2: Develop safety monitoring process	Method 1: Online submission of ADR in clinical trial

	Method 2: Report of ADR within specific timeline as specified by Food and Drug Administration which are - Report SUSAR case within 7 days - Report all ADR case annually
	Method 3: Site monitoring as GCP inspection
Objective 3: to strengthen capacity building in related agencies in order to promote the clinical trial in Thailand	
Strategy 1: Increase the number of qualified investigator	Method 1: GCP Training
	Method 2: Promote and support new investigator working with qualified investigator.
	Method 3: Include GCP in the curriculum of health professional education.
Strategy 2: Develop database and network information related to clinical trial	Method 1: Set up the website containing information related to clinical trial
	Method 2: Promulgate and publish the list of Non-clinical laboratory in Thailand
	Method 3: Be member of International Clinical Trials Registry Platform (ICTRP)
	Method 4: Promote the utmost use of information in TCTR
	Method 5: Set the requirement of registration number of TCTR before published any information in Journal in Thailand

Strategy 3: Increase the number of clinical site with good quality	Method 1: Develop and support Laboratory to have a Good laboratory Practice (GLP).
	Method 2: Support the conduct of clinical trial in Clinical trial Center
	Method 3: Develop the clinical trial management network in order to have the same standard and reduce management cost
Strategy 4: Increase knowledge on research and development of drug or herbal drug	Method 1: Training on research and development process, data requirement for registration

3.2.6 Aspects on the indicators

In order to measure the progress and successful of obtaining the proposed objectives, indicators for each objectives were proposed. The total number of indicators was 28. Four indicators were for the objective of having a standard ethical committee. Sixteen indicators were for the objective of having efficiency and effectiveness of clinical trial control by Food and Drug Administration. Eight indicators were for the objective of capacity building to promote a good quality clinical trial in Thailand. The opinion of the respondents on these indicators were collected and analyzed.

CHAPTER IV

RESULTS AND DISCUSSION

In general, there are three main aspects in assessing the performance or situation, which are structures, processes and outcome. This study which assessed the clinical trial control system in Thailand also used these structures and processes concept. There are many stakeholders involved in clinical trial, which are sponsor, contract research organization, ethical committee, investigator and Food and Drug Administration's personnel. This study focused on the regulatory system on clinical trial. Therefore, the structure and process of Food and Drug Administration and ethical committee were discussed.

Structures are the pivotal inputs for the regulatory system. The structures include a legal framework and an administrative support. Legal framework provides the authority to an organizational body to perform the regulatory functions and to impose any punishments or sanction measures when there are violations of the regulations.

A process also plays an important part to attain the regulatory goal. The process demonstrates the method and the activities to achieve the objective.

The results of this study were separated into four parts as following;

Part I, the situation analysis that was to analyze the opinion on current situation of the clinical trial system in Thailand.

Part II, the designed system analysis was to analyze the opinion on designed system.

Part III, the gap analysis was to identify the gap of current clinical trial control situation and the gap for improvement to reach the designed clinical trial control system.

Part IV, the developing the strategies which was to develop the strategies to be implemented the desired system.

Therefore, the results and discussion would be presented according to the study design as follow;

1. Results of part I: the situation analysis

1.1 Situation from literature review

1.2 Results from the survey

1.2.1 Number of response

1.2.2 Demographic data of respondent

1.2.3 Current experience on the current clinical trial in Thailand

2. Results of part II: the designed system analysis

2.1 Opinion on Food and Drug Administration aspects

2.2 Opinion on Ethical committee aspects

3. Results of part III: the gap analysis and developing strategies

3.1 Gap analysis

4. Results of part IV: the development of strategies

4.1 Information from In-depth interview

4.2 Opinion on the proposed strategies for the designed clinical trial control system

1. Results of part I: the situation analysis

1.1 Situation from literature review

The regulation on importation of investigational drug for clinical trial was issued and implemented in B.E.2532. At the beginning, there was limited information of which only name of applicant, application number, date of submission and date of approval were record in the book. Just only in B.E. 2547, the information technology (IT) was introduced to collect and record the information. The information includes more items such as title of protocol, phase of study, type and amount of investigational drug.

The eligible applicant for importation or manufacture investigational drug could be categorized into two main groups. One was a government agency including academic institutions. Second was private agency, which must have the import license. In addition, private agency included drug company and contract research organization. The data showed that number of application from the government agency was the maximum at 56 in B.E. 2549 and the minimum at 24 in B.E. 2547. Considering with the total number of application, the ration of importation by government agency was decreasing from 25 percent in B.E. 2547 to 14 percent in B.E.2554. On the other hand, the importation by

private agency was increasing every year, especially from the contract research organization.

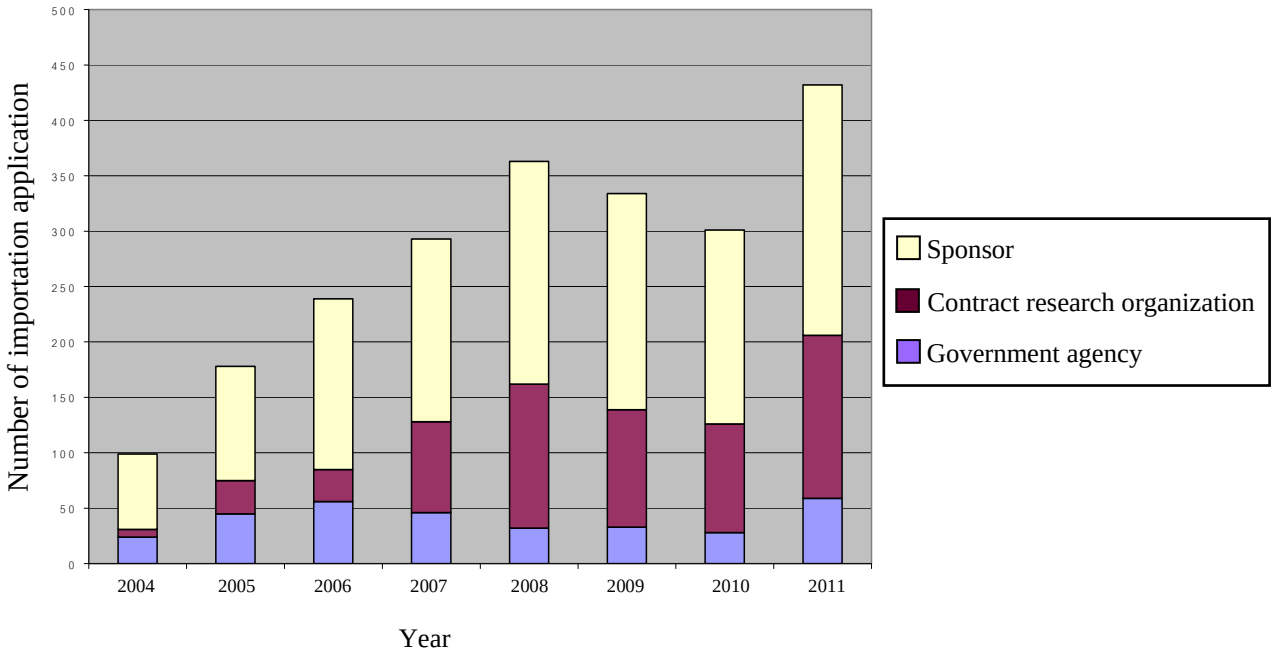

Figure 5: The number of application for investigational drug importation during 2004- 2011 classified by applicants.

The data from Figure 4 showed the number of applications, which were classified into 5 groups as phase I, phase II, phase III, phase IV and unidentified phase, in each year from B.E. 2547 to B.E. 2554. There was 84 percent as unidentified phase application in B.E. 2547 comparing to 0.5 percent of unidentified application in B.E. 2554. This may resulted from the improvement of awareness in collecting and recording data into the IT system.

The number of application for phase I increased from 2 applications which were accounted for 1 percent of total application in B.E.2548 to 14 applications as 4 percent of total application in B.E.2553. In case of phase II, the number of application increased from 24 applications in B.E. 2548 to 80 applications in B.E. 2554. The majority of

applications were for phase III. The maximum number of application for phase III was 320 applications, which accounted for 74 percent from total applications in B.E. 2554.

In summary the number of application was increasing every year and in all phases of clinical trial.

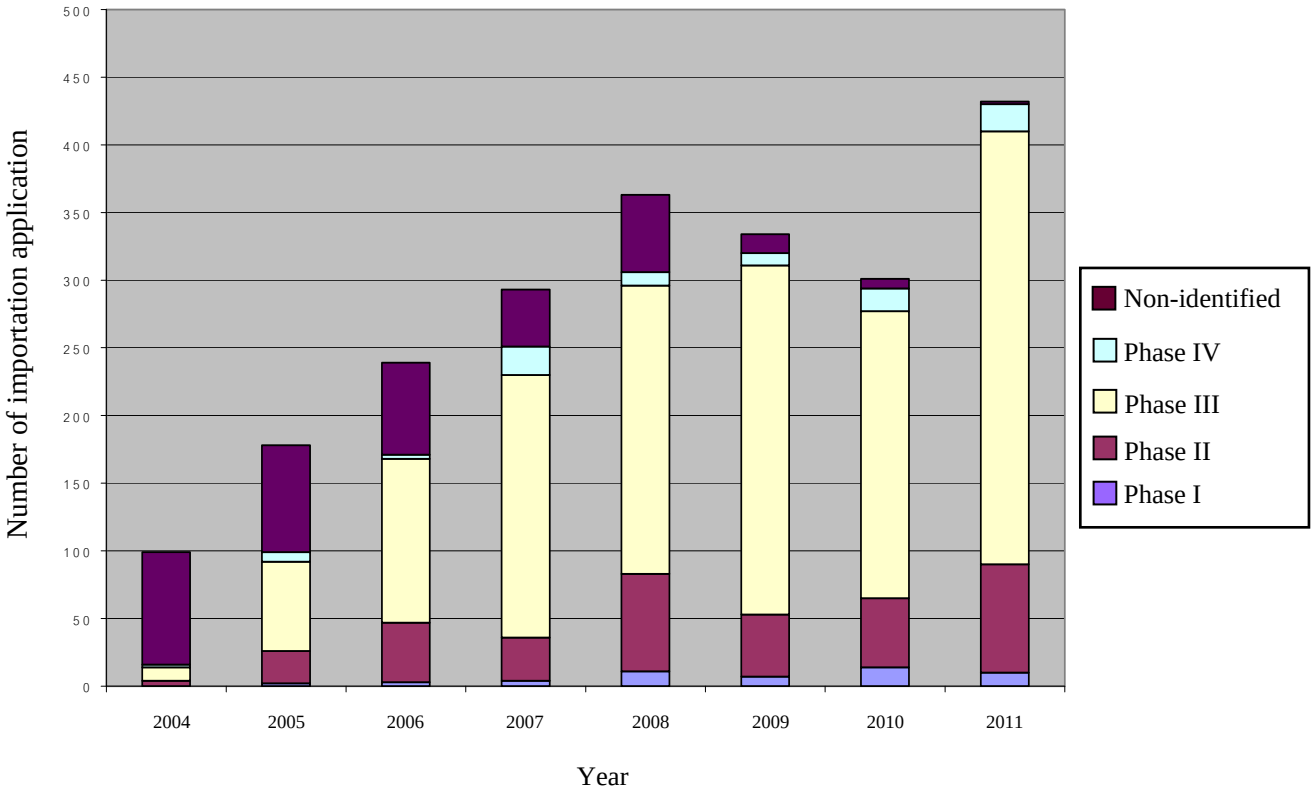

Figure 6: The number of application for investigational drug importation during 2004- 2011 classified by phase of study

1.2 Result from the survey

1.2.1 Number of Response

The questionnaires were distributed to all stakeholders involved in clinical trial. The detailed of questionnaires sent to each group of stakeholders was shown as in Table 2. Total number of the sent questionnaire was 1260. The number of questionnaire sent to the Ethic committee member group was considerable larger than the other group because the study included all ethic committee members who were the member of Forum for Ethical Review Committees in Thailand (FERCIT). FERCIT consisted of any persons

who were interested in an ethical issue. Ethic committee played an important role in controlling clinical trial system due to their reviewing and approving the protocol which leading to the protection of right, safety and well-being of subject.

Table 2: The number of questionnaires distributed to each stakeholders

Stakeholder	Number of questionnaire	Percent of questionnaire
Ethical committee member	756	60.0
Food and Drug Administration's personal	5	0.4
Investigator	454	36.0
Contract Research Organization	15	1.2
Sponsor (Manufacturer or Importer)	30	2.4
Total	1260	100

The 301 completed questionnaires were received whereas there 141 questionnaires were returned due to no-receiver at the address. There were two main causes for no-receiver. Firstly, they were retired from the work. Secondly, they moved to work at other places. Therefore, the response rate of this questionnaire was 26.9 percent.

Table 3: The numbers of questionnaires distributed and received.

	Number of the questionnaires	Percent of questionnaire
Questionnaires distributed by mail	1260	100
Return mail due to no receiver	141	11.2
Filled questionnaires	301	23.9
Response rate	301/(1260-141)	26.9

1.2.2 Demographic data of the respondent

The respondents could be categorized based on their role in the clinical trials such as a sponsor, an investigator, an ethical committee, a contract research organization, a regulator and others. The responses rate within each group and overall were presented as table 4. The response rate within each group was calculated by divided the number of questionnaire received by the number of questionnaire sent.

Table 4: The summary response rate within group and overall (n=301)

Organization	Percent of responses (within group)	Percent of response (overall)
Ethical committee member	13.8	34.8
Food and Drug Administration	100	1.7
Investigator	39.4	59.9
Sponsor	73.3	7.4
Contract Research Organization (CRO)	60	3

1.2.2.1 Stakeholder involved in clinical trial

Considering from the total responses, most of them came from the investigator group which was 59.9 %. The second large of response was from the ethical committee group at 34.8%. Within these two groups, 15.3 % were the respondents who were both the investigators and the ethical committee member. The responses from sponsor and contract research organization are 7.4 % and 3 % accordingly. There were some respondents who also identified themselves as the other groups such as lecturers, coordinator, consultant, quality assurance personal, research team member, research administer and medical journal editor. The response from Food and Drug Administration was accounted for 1.7 %. Considering the responses rate within the group, the study

showed that Food and Drug administration, sponsor and Contract Research Organization had considerably high rate (Table 4).

There were a large number of questionnaires sent to the ethical committee member group but the response rate within the group was only 13.8 %. This resulted from the fact that the questionnaires were sent to the members of the Forum for Ethical Review Committees in Thailand (FERCIT). The FERCIT had a wide range of member's qualification. The member of FERCIT consisted of any persons who were or used to be the member of ethical committee which reviewed the research protocol involved human. The researches involved human are not exclusively the clinical trial using drug products but also some social sciences research. In addition, the clinical researches could cover the research involved with other interventions such as treatment, behavioral education, etc. The responses from the ethical committee were relatively low comparing with the number of questionnaires sent. Nevertheless, the response rate from ethical committee group was the second large group of the study.

The opinions were mainly from the investigator group. This showed that the investigators who were physicians were very interested and highly involved in the clinical trial.

1.2.2.2 Qualification of personal involved in the clinical trial

This study presented the qualification of personal involved in clinical trial in three aspects, which were professional, training, and experiences.

Table 5: The summary qualification of the respondents (n=301)

Qualification	Percent
Professional	
- Physician	58.2
- Pharmacist	12.4
- Nurse	11.4
- Medical technologist	4.3
- Lawyer	0.3
- Others	13.4

Level of education	
- Doctor of Philosophy degree	48.8
- Master degree	37.2
- Bachelor degree	12.6
- Not identify	1.3
Training	
Topic of the training	
- GCP training	79.5
- Ethical related training	69.8
- Others	13.1
- No training	1.7
Number and Type of training	
- training on one topic	44.6
- Training on two topics	42.6
-GCP and Ethical topics	41.7
-GCP and other topics	0.6
-Ethical and other topics	0.3
- Training on more than two topics	10.7

Professional involved in Clinical trial

Most of respondents were physicians at 58.2%. The next groups which had a comparable equivalent were pharmacist and nurse at 12.4% and 11.4% accordingly. The number of the Medical technologist was 4.3%. There was only 0.3% as a lawyer and 13.4% from other professional such as lecturer, social workers, etc.

Level of Education

As mention above the professional involved in the clinical trial were mostly the healthcare professional such as physician, pharmacist, nurse and medical technologist. In addition most of them obtain post-graduation degree. There were 48.8% graduated in the

Doctor of Philosophy degree and 37.2% in the Master degree. Only 12.6% had the Bachelor degree. This showed that people involved in clinical trial were highly educated.

Training

Training is an important role for working especially in the clinical trial. Only basic background on healthcare professional such as physician, nurse and pharmacist is not sufficient because the clinical trial involved with using investigational new drug of which safety and efficacy data are still limited. Many measures should be implemented to ensure the rights, safety and well-being of subject participated in clinical trial be protected as well as the clinical data be credible and scientifically valuable.

There are two pivotal principles which are an ethical consideration and a Good Clinical Practice (GCP) guideline. Firstly, Ethical issue consideration is very important and is the fundamental principle specifically for the ethical committee member. They should have the knowledge, understanding and applying their knowledge in considering whether the protocol submitted for approval are ethical and the subject are protected. Secondly, Good Clinical Practice (GCP) guideline is a standard for designing, conducting, recording and reporting the clinical trial with a consideration of ethical and scientific aspects. Therefore, training of these issues will enable increasing quality improvement of the clinical trial

Data from the survey showed that most of the respondents were trained at least one training program, only 1.7% was not trained. The respondents were trained in Good Clinical Practice (GCP) guideline, Ethical research consideration and other training at 79.5%, 69.8% and 13.1% consecutively. The other trainings that they received were also related to the clinical trial such as clinical trial management and recruitment, clinical trial data management, clinical trial methodology, statistics, GCP audit/inspection and etc. This study showed that Good Clinical Practice (GCP) was the most training program by all stakeholders.

Considering that the more training may increase the quality of the clinical trial, there were 10.7% of the respondents trained for three trainings including the two essential trainings for clinical trial which were the ethical research consideration and the Good Clinical Practice (GCP) guideline, and the others training. Whereas there were 41.6 %

trained in the ethical research consideration and the Good Clinical Practice (GCP). In summary 52.3% of the respondents were trained in the ethical consideration and a Good Clinical Practice (GCP).

As Good Clinical Practice guideline is a fundamental guideline to assure the ethical and scientific quality of conducting clinical trial, therefore all stakeholders involving in clinical trial should have the knowledge and understanding, and be capable to implement accordingly. Even 79.5% were trained in the Good Clinical Practice (GCP) guideline, the training still be needed to cover all stakeholders or persons involved in clinical trial. In addition, Training on ethical research consideration should be promoted not only for the ethical committee group but also for the investigator group. The investigators did not only conduct the clinical trial but sometimes also initiated the clinical protocol. The ethical concerns should be taken by all stakeholders. The priority may be assigned to the stakeholder who makes huge impacts on the ethical, scientific and quality of the clinical trial. The first priority should be the ethical committee group and the investigator group.

Experience in the clinical trial

Time working in the particular role was considered as an experience in that role in this study. There were huge ranges of experience of each stakeholder involved in the clinical trial ranging from 8 months to more than 30 years. However, the majority of experienced time was 10 years for the investigator, ethical committee and other group. For the Food and Drug Administration group, it was a huge range of experience involved in the clinical trial from 7 months to 31 years with the majority at 9 years. The average time of each stakeholder were also calculated and was found that the lowest average time was 6.7 years for the ethical committee group. This showed that the people involved in the clinical trial of drug had a long experience. The detailed was as follows:

Table 6: Number of years experienced in the clinical trial

Stakeholder group	Range (years)	Mode: (years)	Median: (years)	Mean: (years)	Standard deviation
Investigator	1.0-30.0	10	9	9.5	6.4
Ethical committee	1.0-20.0	10	6	6.7	4.0
Sponsor	1.5-20.0	6	7	7.9	4.5
Contract Research Organization	3.0-20.0	3	6.5	8.5	6.0
Food and Drug Administration	0.7-31.0	9	9	11.1	10.4
Others	1.0-30.0	10	9.5	10.1	6.9

1.2.3 Current experiences on Clinical trial Control in Thailand

1.2.3.1 Type of Clinical trial study

Clinical trial study is a study involving human subject in order to investigate pharmacokinetics which are absorption, distribution, metabolism and excretion of the drug, pharmacological or pharmacodynamics of the drug and any adverse events in respect of the drug as well as to ascertain the safety or efficacy of the drug. It includes the study of drug that has been registered and drug that has not been registered and may be under development process.

There were 18.3 % of respondents did not provide information on drug used in clinical trials. This may result from many possible causes. One cause was that the clinical trials were involved with other interventions, not drug. The other was that they were not aware of the type of drug used in their clinical trials.

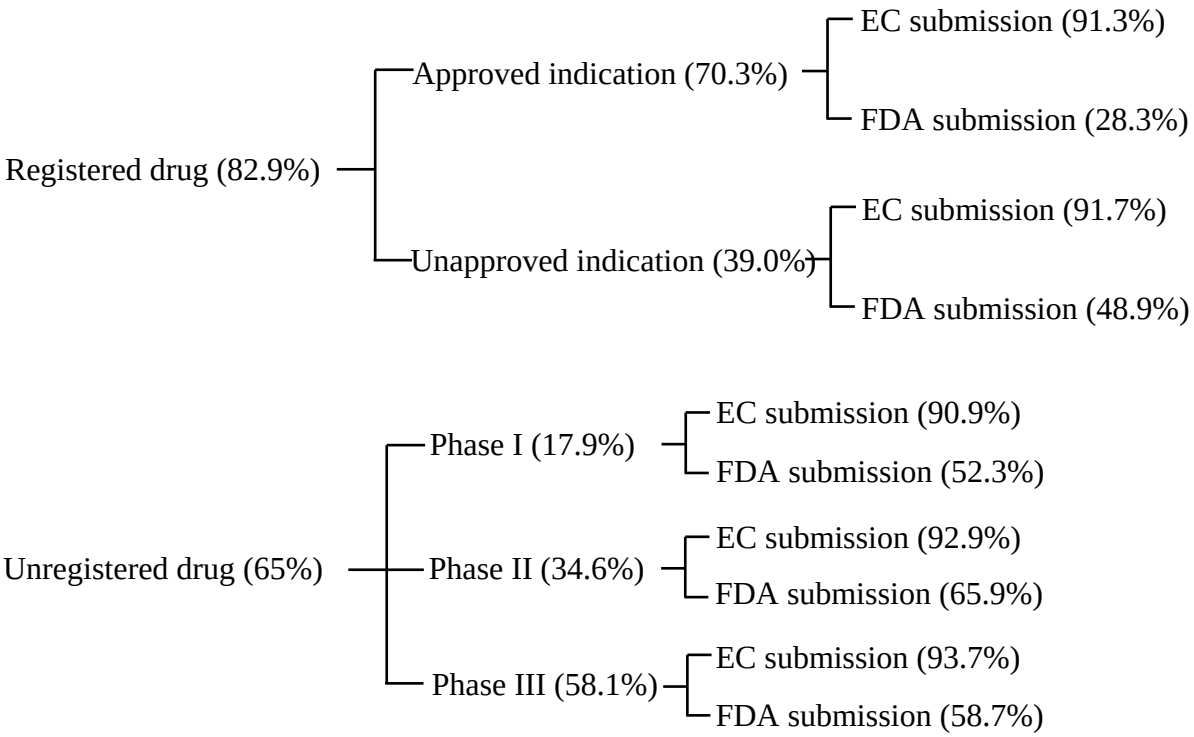

Figure 7: The summary respondents' experience with clinical trials

1.2.3.1.1 Clinical trial study with the registered drug

Registered drugs were the drugs approved by Food and Drug Administration based on sufficient scientific data on quality, toxicity and efficacy. It was considered as safe to be available for patient in the market. 82.9 % of the respondents had experiences in the clinical trial using registered drug. Their involvements in clinical trial with registered drug were not conclusively for the approved indication but also for unapproved indication. The majority was 70.3 % with the approved indication whereas only 39.0% with the unapproved indication.

The unapproved indication implied that there was limited clinical data supported and need more clinical studies. Even there were lower risk than unregistered drug, the precaution and attention on conducting clinical trial could not be avoided.

1.2.3.1.2 Clinical trial study with the unregistered drugs

The definition of unregistered drug in this study was the drug that had not been approved and registered in Thailand. These drugs may be still in the development phase such as under Phase I, II or III clinical study in other countries including country of

origin. In some cases these drugs were in the process of registration and did not get the approval yet. 65.0 % of the respondents had the experience in the clinical trial study with unregistered drug. The clinical trial study of unregistered drug includes clinical trial study in phase I, II and III at 17.9 %., 34.6 % and 58.1% respectively.

Considering the number of clinical trial study of unregistered drug in difference phases of development, the study showed that the clinical trial study in Phase I was a few and the number of the clinical trial study was increasing with the advance phases of clinical trial. The phase I clinical trial study required a special setting and precaution both the facility and healthcare professional because the study was involved the drug with limited safety information especially in human. This phase I clinical trial study is the first introduction of drug into human therefore it must be conducted in the facility with full equipped medical emergency rescue and treatment, mostly in the hospital. In addition, the subject participated in the trial study should be closely monitored at certain period of time for any adverse events.

1.2.3.2 Knowledge on regulatory procedure

Two distinguish aspects of regulatory procedures related to the clinical trial study were Food and Drug Administration's procedure and ethical committee's procedure.

1.2.3.2.1 Food and Drug Administration

Under Drug Acts; Section 79 bis (4), Ministerial Notification No.14:Requirement, process and conditions for importing drug into Thailand with exemption from product licensing issued in B.E.2532, the exemption from registration is only for the purpose of clinical trial/study, analysis, exhibition or donation but has to follow the rule and regulation issued by Food and Drug Administration. The importation of drugs or investigational materials has to submit the application for importation approval from Food and Drug Administration before bringing drugs to be used in the clinical trial. This leads to the fact that the importation of the unregistered drug for the clinical trial study in any phases such as phase I, II or III has to submit application for approval from Food and Drug administration.

The study showed that the respondents submitted the application for

importation approval of registered drug for clinical trial study of unapproved indication and approved indication at 28.32 % and 48.96 % respectively. In the case of unregistered drug, the respondents submitted the application for importation approval for the clinical trial study phase I, II and III at 52.27%, 65.88% and 58.74 % respectively. In summary, only approximately sixty percent submitted for importation approval. The rest did not aware of this regulation. This could result from the fact that the majority of the respondents were investigators and ethical committee members who were not the eligible person for submitting the application for importation.

Even though the investigators were not responsible for drug's importation but they were the key responsible person to conduct the clinical trial. They should know the laws and regulations related to all aspects of conducting clinical trial.

1.2.3.2.2Ethical Committee

Before conducting any clinical trials, the approval from the ethical committee is required. The ethical committee in Thailand could be categorized as Independent Ethics Committee and Institutional Review Board. The definition of Independent Ethic committee (IEC) has been given in ICH-GCP as an independent body constituted of medical/scientific professional and non-medical/non-scientific member, whose responsibility is to ensure the rights, safety and well-being of human subjects are protected as well as the definition of Institutional Review Board (IRB). The difference between IEC and IRB is an independent from the institution, which actually conducts or performs the clinical trial.

Currently there are only a few Independent Ethic committees (IEC) which are the ethic committee of Ministry of Public Health, the ethic committee of institution for development of human research protection and the Central Research Ethics Committee. The study showed that there were 91.3 % and 91.7 % submission to the ethical committee for the clinical trial used registered drug with approved indication and unapproved indication respectively. In the case of unregistered drug, there were 90.9%, 92.9% and 93.7% of submission for clinical trial study phase I, II and III respectively. (Figure 6) This showed that the process of ethical committee approval was well aware and implemented.

The respondents identified that their clinical trials were submitted to Ethic committee of Ministry of Public Health, Ethic committee of Institution for development of human research protection and Central Research Ethics Committee at 32.75, 19.1% and 5 % respectively. Most of the clinical trials were submitted for approval from their Institutional Review Board which accounted for 85.6 %

1.2.3.3 Clinical trial registry

A clinical registry is a system for registering clinical trial. The objective of the system is to strengthen the transparency of the clinical trial, to enhance the accountability of clinical data obtained and to facilitate the access of patient to new drug or new treatment. Mostly they are online-register. The study showed that 61.3% had not registered their clinical trials in any registry systems. The majority of 31.5 % had registered with the United State of America Registry system at www.clinicaltrials.gov. Only 4.2 % have registered at Thai Clinical Trials Registry (TCTR) at www.clinicaltrials.in.th and 3.8% have registered at International Clinical Trial Registry Platform at http://www.who.int/ictrp/en. There were 5.9 % of the clinical trials been registered at the other platforms such as their ethical committees, their research unit or their university.

There is no mandatory measure by Regulatory Authority such as Food and Drug Administration. However some clinical trial studies in Thailand had registered in particular registry platforms mainly at the United State of America Registry system at www.clinicaltrials.gov. This could result from the regulation by U.S. Food and Drug Administration Law that requires certain clinical trials register with the registry. This includes the clinical trials study under investigational new drug application. In addition some clinical trial studies in Thailand are multi-national clinical study therefore they are once registered by any countries will be considered as registered already.

Although the Thai Clinical Trials Registry (TCTR) has been established since B.E.2552 by Clinical Research Collaboration Network (CRCN) and later renamed to Medical Research Network (MedResNet) under the Medical Research Foundation which is non-profit organization. The objective are to promote research transparency, to reduce redundancy, to minimize selective reporting or publication bias and to be a research data

base of clinical researches in Thailand. Only a few clinical studies are register with TCTR. Therefore to promote the transparency and accuracy of related data concerning the clinical trial study especially in Thailand, many measures should be initiated and implemented by related agency.

There are many measures implemented in other countries. Firstly, there is a mandatory measure to register with country's registry platform such as in United State of America, South Africa and India. Secondly, to publish the clinical study result or paper in the medical journal needs the registry of that particular clinical study. For example, The International Committee of Medical Journal Editors (ICMJE) requires the clinical trial registration before considering for publication. 11 Major biomedical journals in India also request the clinical trial registration number before the publication as well. Thirdly, the ethical committee could also support the clinical registry by insisting the registration in the clinical registry of that particular country. This information will be very useful not only for the transparency and the accuracy but also the knowledge of clinical trial situation in the country.

In addition the revised declaration of Helsinki by the World Medical Association (WMA) in October 2008 states that "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject", therefore investigators are obliged to the registry of clinical trial when they declare to comply with the declaration of Helsinki.

As well as the Good Clinical Practice (GCP) guideline states in the principles that "Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki." This leads to the obligation of investigator to make publicly accessible to the data.

1.2.3.4. **Current situation on Good Clinical Practice Inspection or Audit**

An inspection or audit is one of the quality assurance measures to ensure that the clinical trial studies are conducted in accordance with study protocol and ICH-GCP. The inspection or audit is essential for the protection of rights, safety and well-being of the subjects, including the integrity and reliable of the data.

Conducting the clinical trial study was very costly therefore; the sponsor would assure that their studies were well conducted. As shown in Table 7, Sponsor group was the key group, nearly 50 percent, who conducted GCP audit. The next two groups were the Contract Research Organization and the Institutional Ethical Committee at 25.1 and 28.7 percent, accordingly. There was no surprising result because the contract research organization had same roles and responsibilities as the sponsor had delegated them to do. In addition, the Ethical committee whose main role and responsibility is to assure that the right, safety and well being of subject are protected. Therefore, the ethical committee also conducts the GCP audit.

There were three Independent Ethical Committees, which were the Ethics committee of Ministry of Public Health, the Institute for the development of Human Research Protection and the Central Research Ethic Committee. The GCP audits by these committees were only 6.8 percent, 3.9 percent and 2.2 percent, respectively. This showed that the independent review board had performed a few of the audit. Only 6.1 percent were inspected by Food and Drug Administration. Moreover, 32.3 percent had never been inspected or audited.

In summary, there were very few inspections or audits by the concerned regulatory body, Food and Drug Administration and ethical committee especially the independent ethical committee, to assure the quality of clinical trial study in Thailand. This may lead to the quality's problem of the clinical trial study in Thailand. In order to improve or strengthen the clinical trial system in Thailand, the GCP audit or inspection should be increased in both aspects of the number and the quality.

Table 7: The percent of GCP inspection or audit by organization

Inspection or audit Organization	Percent of the inspection
Sponsor	48
Institutional Ethical Committee	28.7
Contract Research Organization	25.1
Ethics committee of Ministry of Public Health	6.8
Food and Drug Administration	6.1
The Institute for the development of Human Research Protection	3.9
Central Research Ethic committee	2.2
Other	5.7
No inspection	32.3

1.2.3.5. Opinion on the other aspects of the current Clinical trial control system

The opinion from all stakeholders were collected using the 5 points likert scale starting from 5 representing the most appropriate/most clear and 1 representing inappropriate/unclear. The questionnaire on current situation part consisted of 17 questions. The detailed of responses were presented as Table 8.

Table 8: The summary of respondents' opinion on the other aspects of the current clinical trial control system by different group of stakeholders.

Items/Mean score ± Std.Deviation	Overall (n=280)	SP (n=18)	PI (n=122)	EC (n=47)	CRO (n=6)	FDA (n=5)	PI and EC (n=42)	Other (n=40)
Composition of EC as stated in ICH-GCP is appropriate	4.0± 0.6	3.9± 0.6	4.0± 06	3.9± 0.6	4.2± 0.8	4.0	4.3± 0.6	4.0± 0.5
Role and Responsibility of involved persons are clearly identified	3.8± 0.7	3.8± 0.7	3.9± 0.6	3.6± 0.8	3.5± 0.8	3.7± 0.6	4.0± 0.7	3.5± 0.6
SOP for EC is appropriate	3.8± 0.7	3.1± 0.8	3.8± 0.7	4.0± 0.6	3.8± 0.8	3.5± 0.6	4.1± 0.6	3.8± 0.6
Procedure of EC approval is appropriate	3.7± 0.7	3.3± 0.5	3.7± 0.7	3.9± 0.6	3.3± 0.8	3.5± 0.6	4.0± 0.6	3.5± 0.8
Training on GCP	3.7± 1.2	3.1± 1.2	3.7± 1.2	4.0± 1.1	3.3± 1.4	3.4± 0.9	4.0± 0.9	3.3± 1.4
Level of Knowledge and Understand of GCP	3.8± 0.8	4.1± 0.6	3.8± 0.7	3.6± 0.9	3.8± 0.4	4.4± 0.5	4.2± 0.6	3.6± 0.8
Level of GCP implementation or compliance	4.0± 0.8	4.2± 0.9	4.1± 0.8	3.8± 0.8	4.2± 0.8	4.6± 0.5	4.3± 0.5	3.8± 0.8
SUSAR report process to FDA is appropriate	3.7± 0.8	3.4± 0.6	3.7± 0.8	3.7± 0.8	3.3± 0.5	4.0± 0.7	3.7± 0.7	3.5± 0.8

Items/Mean score ± Std.Deviation	Overall (n=280)	SP (n=18)	PI (n=122)	EC (n=47)	CRO (n=6)	FDA (n=5)	PI and EC (n=42)	Other (n=40)
Timeline for Progress report to FDA is appropriate	3.5± 0.8	3.4± 0.5	3.6± 0.8	3.5± 0.7	3.3± 0.5	4.0± 2.0	3.4± 0.6	3.4± 0.8
FDA consultation process is appropriate	3.3± 0.8	3.0± 0.8	3.4± 0.9	3.5± 0.7	3.2± 0.8	3.7± 0.6	3.3± 0.6	3.1± 0.8
Guideline for FDA approval of IND's manufacture/importation is clear and easy to follow	3.5± 0.8	3.6± 0.7	3.5± 0.8	3.5± 0.7	3.5± 0.5	4.2± 0.8	3.6± 0.7	3.1± 0.8
Timeline for each step of FDA approval is clearly identified	3.3± 0.8	3.1± 0.9	3.3± 0.8	3.5± 0.7	3.2± 0.4	4.4± 0.5	3.3± 0.6	3.3± 0.8
ADR report process to EC is appropriate	3.7± 0.8	3.1± 0.8	3.8± 0.7	3.8± 0.9	3.5± 0.8	3.7± 0.6	3.9± 0.7	3.7± 0.7
Timeframe for Progress report to EC is appropriate	3.7± 0.7	3.8± 0.4	3.7± 0.7	3.8± 0.9	3.7± 0.8	4.3± 0.5	3.8± 0.8	3.5± 0.7
EC consultation process is appropriate	3.6± 0.8	3.1± 0.8	3.5± 0.8	3.8± 0.7	3.2± 1.0	4.0± 0	3.8± 0.7	3.4± 0.7
Guideline for EC submission is clear and easy to follow	3.8± 0.6	3.5± 0.8	3.9± 0.6	3.8± 0.7	3.8± 0.4	4.0± 0	4.1± 0.6	3.6± 0.6
Timeframe for each step of EC	3.6± 0.9	3.2± 1.0	3.6± 0.8	3.7± 0.8	3.2± 1.3	3.0± 0	3.9± 0.9	3.3± 0.7

Items/Mean score ± Std.Deviation	Over all (n=280)	SP (n=18)	PI (n=122)	EC (n=47)	CRO (n=6)	FDA (n=5)	PI and EC (n=42)	Other (n=40)
consideration is clearly identified								

1.2.3.5.1 Composition of Ethics Committee as stated in ICH-GCP is appropriate.

The survey showed that the composition of Ethics Committee as recommended by ICH-GCP was considered as appropriate (Likert scale 3) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 4.0. The opinions from different groups were similar.

1.2.3.5.2 Role and responsibility of involved persons are clearly identified.

The survey showed that the Role and responsibility of involved persons was considered as less clear (Likert scale 2) to the most clear (Likert scale 5). The overall opinion was more clear at the scale of 3.8. The opinions from different groups were similar.

1.2.3.5.3 Standard Operating Procedure of Ethical Committee is appropriate.

Standard Operating Procedure (SOP) is defined by ICH-GCP as detailed, written instructions to achieve uniformity of the performance of a specific function. In addition SOP is one of the quality measures to assure that the consistency of procedure is maintained which results in the reliability of the process leading to the reliability of the results.

The survey showed that the opinion on Standard Operating Procedure (SOP) of Ethical Committee ranged from inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). However the overall opinion was appropriate leading to more appropriate at the scale of 3.8. The opinions from different groups were similar.

1.2.3.5.4 Procedure of Ethical committee approval is appropriate.

In addition to Standard Operating Procedure (SOP) which provides detailed

information on how to perform the tasks consistently. The overview of the whole processes involved in Ethic committee approval is important too. The steps and time for each particular steps should be logical and rational. The survey showed the process of Ethical approval by Ethical committee was considered as less appropriate (Likert scale 2) to the most appropriate (Lidert scale 5). The overall opinion was appropriate leading to more appropriate at the scale of 3.7. The sponsor group and contract research organization group provided a lower score than other group at 3.3. This represented that they need the improvement in ethical approval procedure.

1.2.3.5.5 Training on GCP

The survey showed that the Training on Good Clinical Practice (GCP) was considered as inappropriate due to no policy on GCP training (Likert scale 1), permit to get training from other organizations (Likert scale 2), unspecific timeframe (Likert cale 3), routine training (every 2-3 years) (Likert scale 4) to the most appropriate as annual training (Likert scale 5). The overall opinion was at the scale of 3.7. They received training every specific timeframe such as every 2-3 years. As mention in ICH-GCP, all concerned parties should have training annually. This study showed that there was a weak point in training.

1.2.3.5.6 Level of knowledge and understand of GCP

The survey showed that the level of knowledge and understand of GCP was considered as not good (Likert scale 1) to the best (Likert scale 5). The overall opinion was better at the scale of 3.8.

1.2.3.5.7 Level of GCP implementation or GCP compliance

The survey showed that the level of GCP Practice or GCP compliance was considered as not good (Likert scale 1) to the best (Likert scale 5). The overall opinion was better at the scale of 4.0.

1.2.3.5.8 SUSAR report system to FDA

As mentioned above, monitoring adverse drug reaction during clinical trial is very important. Stakeholders involved in the clinical trial such as the investigator and the sponsor are obliged to monitor and report the safety to the ethical committee and the competent authority accordingly.

As defined in ICH-GCP, Serious adverse drug reaction is any untoward medical episodes that any doses results in death, life-threatening, being hospitalization or prolong hospitalization, persistent or significant disability, or congenital anomaly or birth defect.

Suspected unexpected serious adverse drug reaction (SUSAR) means any serious adverse drug reaction which the nature or the severity is not consistent with the available drug information such as an investigator's brochure and is reviewed that there may be related to the drug.

Currently Thai Food and Drug Administration requires the manufacturer or importer of investigational new drug to submit an expedited report for Suspected unexpected serious adverse drug reaction (SUSAR). There are a different timeframe for particular cases of SUSAR. If it is a fatal or a life threatening, the report must be submitted within 7 days after first acknowledge by manufacturer or importer. The detailed may be consequently submitted within the next 8 days. In any other cases of SUSAR the report must be submitted within 15 days after first acknowledge by manufacturer or importer.

The survey showed that report system of SUSAR to Thai Food and Drug Administration was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was appropriate leading to more appropriate at the scale of 3.7. The opinions from different groups were similar.

1.2.3.5.9 Time frame for Progress report to FDA

The survey showed that the time frame for progress report to the Food and Drug Administration was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.5 The opinions from different groups were similar

1.2.3.5.10 Procedure of FDA consultation

The survey showed that the Food and Drug Administration's consultation procedure was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.3. The opinions from different groups were similar.

1.2.3.5.11 Guideline for FDA approval of IND's manufacture/importation

The survey showed that the Guideline for FDA approval of IND's manufacture/importation was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.5.

1.2.3.5.12 Timeframe for each steps of FDA approval.

The survey showed that the timeframe for each steps of FDA approval was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.3.

1.2.3.5.13 Adverse Drug Reaction (ADR) report system to the Ethical Committee (EC)

According to the nature of the clinical trial involving the investigational new drugs of which clinical data especially safety and efficacy data are limited, monitoring adverse drug reaction caused by these investigational new drugs is very crucial to assure that safety and well-being of subject are protected. Ethical committee normally requires the adverse drug reaction occurred in the clinical trial report within a defined timeline. The survey showed that the adverse drug reaction report system to the Ethical committee was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was appropriate leading to more appropriate at the scale of 3.7.

1.2.3.5.14 Time frame for Progress report to EC

Report the progress of the clinical trial is essential for monitoring the conduct of the clinical trial. The progress of the clinical trial will show the efficiency of the clinical research team on the whole process starting from recruitment of subject, seeking consent from the subject, providing intervention as described in the protocol, follow-up process, interim data analysis and the end report

The survey showed that the time frame for progress report to the Ethics Committee was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.7

1.2.3.5.15 EC consultation process

The survey showed that the Ethics Committee's consultation process was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.6.

1.2.3.5.16 Guideline for EC submission

The survey showed that the Guideline for EC submission was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion is more appropriate at the scale of 3.6. It is clear and easy to follow.

1.2.3.5.17 Timeframe for each steps of EC consideration is clearly identified

The survey showed that the timeframe for each steps of EC consideration was considered as inappropriate (Likert scale 1) to the most appropriate (Likert scale 5). The overall opinion was more appropriate at the scale of 3.6.

In view of the overall opinion on the other aspects of the current clinical trial control system, this study showed that all aspects got the higher score than appropriate (Likert scale 3). Some of the aspects which were the composition of the ethical committee and the level of GCP implementation had a higher score of more appropriate (Likert scale 4).This could be interpreted that the current situation of the clinical trial in Thailand was considerable appropriate. Due to the range of opinion on the aspects was wide from inappropriate (Likert scale 1) to most appropriate (Likert scale 5), this showed that there were some gaps need to be improved.

In the view of defining these aspects into structure and process component, there were four aspects as structure component and thirteen aspects as process component. There were also categorized into group items based on organization body involved which were Food and Drug Administration (FDA) and ethical committee (EC). The detailed of the components, group items and the opinions on each particular item and the group item were as following table 9;

Table 9: The summary opinions on structure and process aspects

Components	Group item	Items
Structure (over all) (mean=3.8,std.deviation=0.5)	Structure (General) (mean=3.9,std.deviation=0.5)	Composition of EC as stated in ICH-GCP is appropriate (mean=4.0)
		There should be the law that identify the role, responsibility of all stakeholders involved in clinical trial, approval, investigate, suspend, cancel (mean=3.8)
	Structure (EC related) (mean=3.7,std.deviation=0.7)	SOP for EC is appropriate (mean=3.8)
		Procedure of EC approval is appropriate (mean=3.7)
Process (over all) (mean=3.7,std.deviation=0.5)	Process (General) (mean=3.9,std.deviation=0.8)	Training on GCP (mean=3.7)
		Level of Knowledge and Understand of GCP(mean=3.8)
		Level of GCP implementation or compliance (mean=4.0)
	Process (EC related) (mean=3.7,std.deviation=0.6)	ADR report process to EC is appropriate (mean=3.7)
		Timeframe Progress report to EC is appropriate(mean=3.7)
		EC consultation process is appropriate(mean=3.6)
		Guideline for EC submission is clear and easy to follow(mean=3.8)
		Timeframe for each step of EC consideration is clearly identified (mean=3.6)
	Process (FDA related) (Mean=3.5,std.deviation=0.7)	SUSAR report process to FDA is appropriate (mean=3.7)

Components	Group item	Items
		Timeline for Progress report to FDA is appropriate.(mean=3.5)
		FDA consultation process is appropriate (mean=3.3)
		Guideline for FDA approval of IND's manufacture/importation is clear and easy to follow (mean=3.5)
		Timeline for each step of FDA approval is clearly identified (mean=3.3)

The opinion on the over all aspect of the structure component was 3.8 on the Likert scale, which showed that it was considered as likely more appropriate. Whereas the over all aspect of the process was 3.7 that was lower than the structure aspects. Considering the opinions on these two aspects, they were comparable equivalent. There was no urgent need to focus only on the structural or the process aspects for improving the situation. Nevertheless, the efforts should be made to improve or strengthen the system both aspects simultaneously.

The data from the group items showed that the process components related to Food and Drug Administration got the minimum score at 3.5. This showed that the process components related to Food and Drug Administration was a priority area for improvement.

2. Results of Part II: the designed system analysis

The conducting of clinical trial in Thailand has evolved especially over the past ten years. The clinical trial control system has being continuously improved not only in Food and Drug Administration but also in other stakeholders. However, the pivotal issues are related to the authorities, which are Food and Drug Administration and Ethical Committee. Some amendments in the clinical trial control system were proposed in order to improve the efficiency of the system. The questionnaires on the designed system with some specific issues were sent to all stakeholders. These issues were categorized based

on organization body involved as Food and Drug Administration (FDA) and ethical committee (EC). There were eight issues for FDA and six issues for EC. In addition, these were also categorized due to the process and structure aspects. There were six issues as structure aspect and eight issues as process aspect. The summary opinions on designed issues were presented in Table 12 and Table 13.

2.1 Opinion on the designed clinical trial control system

2.1.1 Opinion on Food and Drug Administration aspects.

There were eight proposed issues related to Food and Drug Administration. The study showed that most of proposed issues were agreeable by stakeholders with more than 80%. Only the consultation system and the report of progress or ending or final report were 78.6 % and 77.0%, respectively. The respondents thought that Food and Drug Administration had no responsibility to provide the consultation in developing the clinical protocol as well as had limited resources on the qualified experts.

Table10: The summary opinions on proposed issued related to Food and Drug Administration

Issues	Agreeable (percent)
Issues related to Food and Drug Administration	
Scope of the application for manufacture or importation of drugs for clinical trial is limited to the drugs that are not registered in Thailand or the registered drug with unapproved or new indication, new dose or new group of patients.	87.2
There should be the law that identify the role, responsibility of all stakeholders involved in clinical trial, approval, investigate, suspend, cancel	88.1
Thailand should formally set a Good Clinical Practice (GCP) ICH-GCP as a standard for the conduct of clinical trial.	93.9

Issues	Agreeable (percent)
The application for manufacture or importation of drug for clinical trial includes these documents: -Label (Thai or English) -Package insert (for registered drug) -Investigator brochure (For unregistered drug) -Patient information sheet (Thai) -Protocol summary (Thai) -Protocol (Thai or English) -Chemical, Manufacture and Control documents Note: No Ethical committee approval certificate required.	84.5
The quality system should be in place and approved by third party.	90.1
The consultation system for developing and improving protocol should be in place.	78.6
The manufacturer or importer should be responsible to report any adverse drug reaction related to the clinical trial.	90.7
The manufacturer or importer should be responsible to report the progress of the clinical trial including the end of study or final report.	77.0

2.1.2 Opinion on Ethical committee aspects

There were six proposed issues related to ethical committee. The study showed that three of proposed issues were agreeable by stakeholders with more than 80 %. Whereas another three proposed issues which were the law governing ethical committee, the clinical trial registry and accreditation body were 77.2 %, 79.2%. and 79.5 % agreeable.

Table 11: The summary opinion on proposed issued related to Ethical committee

Issues	Agreeable (percent)
Issues related to Ethical committee	
There should be the law that identify the composition, role, operation and responsibility of Ethical committee inspection ,disqualify	77.2
The quality system should be in place and approved by third party.	88.3
A specific organization should be set up for the accreditation of Ethical committee.	79.5
The investigator should be responsible to report any adverse drug reaction related to the clinical trial.	93.6
The investigator should be responsible to report the progress of the clinical trial including the end of study or final report.	94.0
Thailand should require all clinical trails registered at the Thailand Clinical Trial registry.	79.2

2.1.3 Opinion on the structure and process aspects of the system

In the view of defining these proposed issues into structure and process components, the detailed of the components and the opinions on each particular item were presented in Table 12.

Table 12: The summary opinion on proposed issued related to the structure and process

Issues	Agreeable (percent)
Issues related to Structure	
Thailand should formally set a Good Clinical Practice (GCP) ICH-GCP as a standard for the conduct of clinical trial.	93.9
Thailand should require all clinical trails registered at the Thailand Clinical Trial registry.	79.2
Scope of the application for manufacture or importation of drugs for clinical trial is limited to the drugs that are not registered in Thailand or the registered drug with unapproved or new indication, new dose or new group of patients.	87.2
There should be the law that identify the role, responsibility of all stakeholders involved in clinical trial, approval, investigate, suspend, cancel	88.1
There should be the law that identify the composition, role, operation and responsibility of Ethical committee inspection ,disqualify	77.2
A specific organization should be set up for the accreditation of Ethical committee.	79.5
Issues related to Process	
The application for manufacture or importation of drug for clinical trial includes these documents: -Label (Thai or English) -Package insert (for registered drug) -Investigator brochure (For unregistered drug) -Patient information sheet (Thai) -Protocol summary (Thai)	84.5

Issues	Agreeable (percent)
-Protocol (Thai or English) -Chemical, Manufacture and Control documents Note: No Ethical committee approval certificate required.	
The quality system in Food and Drug Administration should be in place and approved by third party.	90.1
The manufacturer or importer should be responsible to report any adverse drug reaction related to the clinical trial.	90.7
The manufacturer or importer should be responsible to report the progress of the clinical trial including the end of study or final report.	77.0
The consultation system for developing and improving protocol should be in place.	78.6
The quality system in Ethical committee should be in place and approved by third party.	88.3
The investigator should be responsible to report any adverse drug reaction related to the clinical trial.	93.6
The investigator should be responsible to report the progress of the clinical trial including the end of study or final report.	94.5

2.2 Opinion on an aspect of appropriate organization for governing particular law and regulations in the designed clinical trial control system

2.2.1 Responsible organization for the Law concerning ethical committee

The law concerning human research, which particularly focuses on ethical committee, has been drafted and is under enacting process. The study showed that National Research Council of Thailand was the preferable agency to be responsible for enacting and governing this Human research Acts.

Table 13: The summary opinion on organization governing ethical committee

Organization	Agree (percent)
National Research Council of Thailand	51.2
Ministry of Public Health	43.7
Other	20.5

However, there were many suggestions on other organizations or agencies that could be the responsible body for governing this human research law. Some suggestions were both of Ministry of Public Health and National Research Council of Thailand, or a new committee or new organization, which involved other health professionals such as medicines council, pharmacist council, nurse council, dentist council and technical council. In addition, some proposed to include lawyer, academia, representative from institutional review board and lay person to be the member of new board governing this new law.

2.2.2 Responsible organization for the Law concerning Good Clinical Practice

The study showed that National Research Council of Thailand had a little higher agreement than Ministry of Public Health to be a responsible organization for issuing and governing law related to Good Clinical practice. The detailed of responses were presented in Table 14.

Table 14: The summary opinion on organization governing Good Clinical Practice

Organization	Agree (percent)
National Research Council of Thailand	44.5
Ministry of Public Health	41.1
Medicines Council	24.7
Other	14.4

2.2.3 Responsible organization for Thailand Clinical Trial Registry

The study showed that National Research Council of Thailand should be a responsible organization for Clinical Trial Registry of Thailand. Currently Medical Research Foundation is the founder of Thai Clinical Trial Registry (TCRT). Therefore, the cooperation between National Research Council of Thailand and Medical Research Foundation should be explored. The detailed of responses were presented in Table 15.

Table15: The summary opinion on organization governing Thailand Clinical Trial Registry

Organization	Agree (percent)
National Research Council of Thailand	46.6
Ministry of Public Health	32.1
Medical Research Foundation	25.2
Other	9.3

3. Result of Part III: Gap analysis

In general, there are three main aspects in assessing the performance, which are structures, processes and outcome. This could also be used in assessing the clinical trial control system in Thailand. There are many stakeholders involved in clinical trial, which are sponsor, contract research organization, ethical committee, investigator and Food and Drug Administration's personnel. This study focused on the regulatory system on clinical trail. Therefore, the structure and process of Food and Drug Administration and ethical committee were discussed. The opinions on current situation of clinical trial and designed clinical trial system were also discussed.

3.1 Structure aspects

3.1.1 Structure aspect related to Food and Drug Administration

Structures are the pivotal inputs for the regulatory system. The structures include a legal framework and an administrative support. Legal framework provides the authority

to an organization to perform the regulatory functions and to impose any punishments or sanction measures when there are violations of the regulations. Currently there is only Drug acts (B.E.2510), particularly Ministerial Notification no.14 (B.E.2532) : Requirement, process and conditions for importing drug into Thailand with exemption from product licensing and Food and Drug Administration's notification (B.E.2549) which governing the importation and manufacture of investigational drug for clinical trial. These Food and Drug Administration's regulations outline the measures to have a good clinical trial control such as requiring Good Clinical Practice (GCP), list of recognized ethical committee, GCP inspection, SUSAR report and annual report. However, there is no measure to punish the violation or revoke the approval. Only if there is a serious safety issue that Food and Drug Administration is able to stop the use of those investigational drugs.

The survey showed that most of the respondents (more than eighty percent) agreed with the designed system to have the regulations covering role, responsibility, compliance of related stakeholders including type of clinical trial of which need approval from Food and Drug Administration. Hence this was one of priority areas that would fulfill all stakeholders' need.

There is no law or regulation concerning the standard of Good Clinical Practice. Currently ICH-GCP is practically implemented by concerned parties on the voluntary basis. Voluntary measure has an inferiority that there could be someone not abide by or complied with this measure without any punishments. The study showed that ICH-GCP currently was well understood and implemented by all stakeholders but the legalized of this standard was still needed to ensure the compliance by the stakeholders.

3.1.2 Structure aspect related to the ethical committee

A group of interested institutional ethical committee has established a forum for ethical review committee in Thailand (FERCIT) in 2000. The objectives of FERCIT are to promote and develop subject protection, to promote and develop ethical committee control system, to exchange knowledge and experiences among members and international agency. There is no legal framework to govern the ethical committee.

This study showed that current composition of ethical committee was considered more appropriate. However the law concerning control of ethical committee and a responsible agency was less preferable with only at most 79.5 percent. Nevertheless the law and regulation concerning was essential to assure the quality, transparency and accountability of ethical committee was needed. In addition the organization of which responsible for this law needed to be identified including the mechanism of accreditation.

3.2 Process aspects

A process also plays an important part to attain the regulatory goal. The process demonstrates the method and the activities to achieve the objective. The study showed that the current processes by Food and Drug Administration and ethical committee were likely more appropriate. In addition the improvements with more details in the process as mentioned in designed system were agreeable. There were concerns on some new proposed processes that may cause difficulties in implementation such as reporting within designated timeline and consultation system. The detailed of opinions on current and designed system were presented in Table 16.

In summary the opinion on current situation showed the average scale of appropriateness at less than 4 (more appropriate). In order to have a good clinical trial control, all items or aspects should have at least the score of more appropriate. Therefore there were the gaps for improvement in all areas. The priority would be assigned to the items with lowest scale, highest percent of agreement or both.

Table 16: The summary opinion on current and designed system

Opinion on current situation	Likert Scale	Opinion on the designed system	Agree (percent)
Structure (general)			
		Thailand should formally set a Good Clinical Practice (GCP) ICH-GCP as a standard for the conduct of clinical trial.	93.9

Opinion on current situation	Likert Scale	Opinion on the designed system	Agree (percent)
		Thailand should require all clinical trails registered at the Thailand Clinical Trial registry	79.2
Composition of EC as stated in ICH-GCP is appropriate	4.0		
There should be the law that identify the role, responsibility of all stakeholders involved in clinical trial, approval, investigate, suspend, cancel	3.8		
Structure (FDA)			
		Scope of the application for manufacture or importation of drugs for clinical trial is limited to the drugs that are not registered in Thailand or the registered drug with unapproved or new indication, new dose or new group of patients.	87.2
		There should be the law that identify the role, responsibility of all stakeholders involved in clinical trial, approval, investigate, suspend, cancel	88.1
System(EC)			
		There should be the law that identify the composition, role, operation and responsibility of Ethical committee inspection ,disqualify	77.2

Opinion on current situation	Likert Scale	Opinion on the designed system	Agree (percent)
		A specific organization should be set up for the accreditation of Ethical committee.	79.5
SOP for EC is appropriate	3.8		
Procedure of EC approval is appropriate	3.7		
Process (General)			
Training on GCP	3.7		
Level of Knowledge and Understand of GCP	3.8		
Level of GCP implementation or compliance	4.0		
Process (FDA)			
		The application for manufacture or importation of drug for clinical trial includes these documents: -Label (Thai or English) -Package insert (for registered drug) -Investigator brochure (For unregistered drug) -Patient information sheet (Thai) -Protocol summary (Thai) -Protocol (Thai or English)	84.5

Opinion on current situation	Likert Scale	Opinion on the designed system	Agree (percent)
		-Chemical, Manufacture and Control documents Note: No Ethical committee approval certificate required.	
		The quality system should be in place and approved by third party.	90.1
SUSAR report process to FDA is appropriate	3.7	The manufacturer or importer should be responsible to report any adverse drug reaction related to the clinical trial.	90.7
Timeline for Progress report to FDA is appropriate	3.5	The manufacturer or importer should be responsible to report the progress of the clinical trial including the end of study or final report.	77.0
FDA consultation process is appropriate	3.3	The consultation system for developing and improving protocol should be in place	78.6
Guideline for FDA approval of IND's manufacture/importation is clear and easy to follow	3.5		
Timeline for each step of FDA approval is clearly identified	3.3		
Process (EC)			
		The quality system should be in place and approved by third party.	88.3
ADR report process to EC is appropriate	3.7	The investigator should be responsible to report any adverse drug reaction related to the clinical trial.	93.6

Opinion on current situation	Likert Scale	Opinion on the designed system	Agree (percent)
Timeframe for Progress report to EC is appropriate	3.7	The investigator should be responsible to report the progress of the clinical trial including the end of study or final report.	94.5
EC consultation process is appropriate	3.6		
Guideline for EC submission is clear and easy to follow	3.8		
Timeframe for each step of EC consideration is clearly identified	3.6		

4. Results of part IV: the developing strategies

4.1 Information from in-depth interview

Four representatives from sponsor, investigator, contract research organization (CRO) and Food and Drug Administration were interviewed on these main topics which were current situation, problems, desired system and suggestions.

4.1.1 Opinion on current situation

All interviewees thought that the clinical trial control environment had been improved over the years especially after the year 2000 which all related stakeholder groups joined together and formed a group, later became a Thailand Towards Excellence in Clinical trials (ThaiTECT). However, some expected that the improvement should have been faster and more effective than current situation.

Most of the clinical trials conducted in Thailand were sponsored by drug's company especially the multi-national drug company. These resulted in most of tested drug being investigational drug or innovative drug from the developed countries. There were few clinical trials using drug developed in the country such as herbal or traditional medicines.

There were increasing numbers of the clinical trials in Thailand, both sponsors-initiated and investigator-initiated. In addition, the sponsor-initiated clinical trials included multi-national clinical trials and local clinical trials. Each type of clinical trials

whether sponsor or investigator initiated had different pitfalls. Most of sponsor-initiated clinical trials had the well-designed protocol because they had resources to involve people from multidisciplinary. However if it was a multi-national protocol it might not be implemented as an original protocol due to specific local situation such as cultural, professional practice and equipments which needed some amendments. If it was the sponsor-initiated protocol for local trials, the results of the study had a limited used, not for regulatory purpose. There was no clinical data submission from local trials for regulatory purpose such as amendments of indication, dose regimen, precaution or adverse drug reaction.

The role of contract research organization (CRO) in Thailand were both as a coordinator of the clinical trial among multi sites and a clinical research center. Some contract research organizations (CRO) also helped investigators develop clinical trial protocol. There were more clinical research center (CRC) established in recent years, mostly within or attached with universities especially which had faculty of medicines.

The ethical committee approval process was improved over the years. Many ethical committees were surveyed by Strategic Initiative for Developing Capacity in Ethical Review/ Forum for Ethical Review Committees in Asian and Pacific regions (SIDCER/FERCAP) which showed that these ethical committee had a good quality review system. Even though FERCIT was established in 2000 it was only a voluntary cooperation among ethical committees.

Investigational drug unit, pre-marketing division, Bureau of drug control of Food and Drug Administration was a responsible unit for approval the manufacture and importation of investigational drug for clinical trial and GCP inspection. There were only few staffs. The most priority was the approval for manufacture or importation of investigational drug. Then the priority areas were set for GCP inspection. Currently GCP inspection focused on the drug accountability, number of subjects, enrollment and consent process, SUSAR case report and protocol conformity. Quality system such as standard operating procedure (SOP) was implemented and annually audited by Food and Drug Administration.

4.1.2 Opinion on problems

Bioequivalence study is considered as a clinical trial because it involves humans. However, currently the importation or manufacture an investigational drug for bioequivalence study is under the regulation of importation or manufacture the drug sample for registration purpose which requires only certificate of free sale (in case of importation) and a sample of insert and label. There is no requirement on submitting the protocol and the ethical committee approval as other clinical trials. In summary, there is different requirement for clinical trials with different purpose.

There were only ten ethical committees recognized by Food and Drug Administration which were considered as not enough and not transparency. The ethical committees in other institutes especially involved with health care had no opportunity to be recognized. The criteria for recognition of ethical committee were not publicly available. The limited number of recognized ethical committee became a bottlenecked for approval process and caused a delay in conducting the clinical trial.

The timeline of Food and Drug administration approval as 20 working days was considered as appropriate but the assurance should be made that all applications were within this timeline. The current approval was based on the protocol with specific site, number of subject and the amount of drug used within one year. In case of the re-submission of the same protocol with the different site and number of subject should take less than 20 working days.

Timeline was the majority concerns of sponsor, contract research organization and investigator. They wanted to know exactly when ethical committee and Food and Drug Administration would approve their protocols in order to plan for conducting the trial as soon as possible. They said time was the money. The longer the process was, the more money spent in the trials.

Developing the clinical trial protocol especially for the local trials was also a problem. The process of developing the protocol involved many disciplines including toxicology, pharmacology, epidemiology, statistics, physician, etc. They need to work together. There was a lack of cooperation among these groups of expertise. Even there were some clinical research centers to solve the problem it was still needed more

collaboration among multi-disciplinary and made the information publicly available to any other persons interested.

There were many physicians interested in being investigator or co-investigator. However being a good investigator or co-investigator was not only being a good physician but also being a good compliance with GCP and devoted enough time for the study including record and review data. Some sponsors had programs to support new investigators by introducing them to work with experienced investigators or supporting their trials. The support included not conclusively developing the protocol, training, drugs, etc.

Data management and data analysis was also a problem. A lot of data were collected from the clinical trial therefore only the investigator may not be able to manage or analyze the results. If the trial was multi-site clinical trial, there were more data collected and more difficulty in managing and analyzing. There was a need for organization with the expertise and resource in data management and analysis.

4.1.3 Opinion on designed system

The designed system was a few changes to the current system. These changes were intended to improve and provide more detailed information. Some could be immediately implemented whereas some may be implemented later or adjusted before.

Quality system was a pivotal component for assuring the quality system. Food and Drug administration and recognized ethical committees currently had the quality system and SOP that could ensure the quality of the review process. The quality certification by third party was not necessary however; the assurance of compliance was needed.

Clinical trial registry was a good measure to be more transparency about the conducting and the result of clinical trial. If Thailand would like to implement Thailand Clinical trial registry as a mandatory measure to all clinical trial conducted in Thailand, the rational should be made and the duplication with other registries had to be avoided.

4.1.4 Opinion on suggestion

Any changes related to the regulatory aspects of clinical trial control should not be time consuming but still fulfill the role, responsibility and mission. The rational for each regulatory measure should be clarified and notified all concerned parties. As the limitation of staff in investigational drug unit, Bureau of Drug control, Food and Drug Administration, another process or procedure should be explored such as working as a committee, working as external expert or delegate some responsibility to other units or organizations.

There was no formal consultation process for clinical trial development with Food and Drug Administration. If Thailand would like to have local herbal drug or traditional drug market in other countries, the scientific evidence from clinical study were essential. Therefore, the consultation process was necessary. In addition to have a successful drug development, a designated unit or organization, which was responsible for over all planning, overview, risk and management decision had to be established. This could be national and institutional level.

4.2 Result from the survey

The information obtained from gap analysis and in-depth interview were used in developing the second questionnaire: the opinion on development clinical trial control in Thailand.

4.2.1 Number of Response

The questionnaires were distributed to all participants at the ThaiTECT meeting, an annual meeting of stakeholders involved in clinical trial. The number of participant at the meeting was 166 and the number of filled questionnaire was 54. The response rate was 32.5 %. The demographic detailed of participants who answered the questionnaire were showed in Table 17.

Table17: The summary demographic data from filled questionnaire

Demographic data	Number of response (percent)
Stakeholders	
- Sponsor	35.2
- Investigator	13.0
- Ethical committee member	20.4
- Contract Research Organization	20.4
- Food and Drug Administration personal	3.7
- Other	7.4
Professional	
- Physician	13.0
- Pharmacist	44.4
- Nurse	22.2
- Medical technologist	3.7
- Other	16.7
Level of education	
- Doctor of Philosophy degree	16.7
- Master degree	57.4
- Bachelor degree	25.9
Number of years involving with the clinical trial	
- less than or equal to 5 years	33.3
- > 5 – 10 years	31.5
- > 10 – 15 years	18.5
- > 15 – 20 years	13.0
- > 20 – 25 years	3.7

4.2.2 Opinion on the objective of the clinical trial control system

The study showed that the respondents all agreed on three objectives of the clinical trial control system. Firstly, the ethical committee should be over sighted in order to ensure the standard of ethical consideration. Secondly, the control of clinical trial by Food and Drug administration should be effective. Lastly, capacity building in all related agencies should be strengthened and implemented in order to promote the clinical trial in Thailand. The important and feasibility aspects of proposed strategies and method were studied using the likert scale from 3 to 1 representing most, medium and low important or feasibility. Considering the important and feasibility aspects, there were no significant difference among these objectives. Therefore, the strategies and methods for these particular objectives should be implemented simultaneously. However, each particular strategy and method had different important and feasibility. The priority for implementation then was based on the level of important and feasibility provided by the respondents.

4.2.3 Opinion on the strategies and method of particular objectives

4.2.3.1 To have a standard on Ethical committee

The survey showed that the respondents totally agreed with the strategy of having an accreditation or recognition system for ethical committee and 96 percent on strategy of national standard on ethical committee. The priority of methods for particular strategy based on agreeable, important and feasibility consecutively was presented in Table 18.

Normally standard must be established before any accreditation or recognition. However, this study showed that an accreditation or recognition was a priority to be implemented. This resulted form many reasons. Firstly, one of current requirements for importation or manufacture of investigational drug for clinical trial was an ethical approval from the recognized ethical committee. There were only ten ethical committees recognized by Food and Drug Administration. Therefore, it was an urgent need to increase the number of recognized ethical committee in order to avoid the obstacle as a bottle neck for conducting clinical trial in Thailand. The feasibility was relatively high due to many organization were trying to implement the accreditation or recognition system. Food and drug administration drafted the criteria for recognition of ethical

committee in 2011 and collected comments from concerned stakeholders. It was revised many times but up until now the criteria has not been issued yet. Another agency, national research council of Thailand has also been working on establishing national ethics committee accreditation system of Thailand (NECAST).(Sopit,2013)

Secondly, even though the standard guideline on conducting clinical trial such as Good clinical practice (GCP) was not formally issued by any agencies, there was a memorandum of understanding among stakeholders such as ministry of public health, ministry of education and Pharmaceutical Research and Manufacturer association (PReMA) to conduct the clinical trial complied with ICH-GCP standard. This demonstrated that the standard guideline as ICH-GCP was informally accepted and implemented in Thailand since 2000.

In order to legalize law related to clinical trial, a human research act has been drafted. (Ministry of Public Health, 2010) The acts has still been in the public hearing process in order to collect any concerns from all stakeholders because there are some controversial issues need to be resolved. In addition, National research council of Thailand has draft another human research act. (Soottiporn,2013) Then, there will be more discussion on human research acts during the process of enacting the acts by the parliament. Therefore, the feasibility to have the acts in the near future is considerable low.

Hence, Food and Drug administration should take a leading role in order to have a standard ethical committee involving in clinical trial by issuing the regulation on criteria for recognition of ethical committee and the standard guideline of GCP for conducting clinical trial. When NECAST is formally established, the cooperation between Food and Drug administration and national research council of Thailand should be explored in order to complement each other’s role and responsibility and to reduce the redundant works.

Table 18: Strategy and method for the objective of standard ethical committee.

Strategy and Method	Agree (percent)	Important (Likert scale)	Feasibility (Likert scale)	Priority (Important x Feasibility)
Strategy 1: An accreditation or recognition system	100	2.79	2.45	6.84
Method 1: Define or set up a specific agency responsible for accreditation or recognition	98	2.73	2.32	6.33
Method 2: Monitor periodically every two years	91.7	2.48	2.26	5.60
Strategy 2: National standard for Ethical committee	96	2.76	2.16	5.96
Method 1: Each institution formally establishes an ethical committee or recognizes other institution's ethical committee complied with ICH-GCP standard.	100	2.73	2.45	6.69
Method 2: Food and Drug administration issues the regulation on ethical committee recognition.	98	2.76	2.33	6.43
Method 3: Thailand has Human Research Acts.	96	2.76	2.16	5.96

4.2.3.2 To have efficient clinical trial control by Food and Drug administration.

There were two proposed strategies to improve the efficiency of clinical trial control by Food and Drug administration. The survey showed that the respondents totally agreed with the strategy on developing the standard, procedures and evaluation, and 98

percent agreed on developing safety monitoring process. The priority of proposed methods for particular strategy based on important and feasibility was presented in Table 19.

The study showed that the respondents thought that quality assurance system such as standard, SOP and criteria for evaluation were comparatively high important. In addition, the issuing of regulation related to clinical trial such as type of investigational drug for clinical trial use and role and responsible of all concerned stakeholders were also considered as relatively high important and feasibility. On the other hands, online submission of both application and report of Adverse Drug Reaction (ADR) were considered as likely high important but likely medium feasibility. This may result from the amount and complexity of documents required for application and the experience of respondents in online submission of ADR report of marketed drug. The respondents provided the suggestion that the system should be friendly-used for user. In order to introduce and implement online submission effectively, all these factors must be considered when designing and preparing the computer system.

If structure and process aspects were used in identifying these proposed methods, to issue the regulations and to require the registration number of TCTR in the application were the structure aspect. The others were considered as the process. The results showed that both of them were important for the development and improvement of clinical trial control by Food and drug Administration.

To legally issue the new regulation or requirement may take times and efforts. However, the administrative measures could be used in order to solve, to prevent any unwanted incidences or to improve the work efficiency. Therefore, to identify the type of investigational drug used and phase of clinical trial could be implemented by improving the checklist during document screening when submitting application at Food and Drug Administration. Nevertheless, the legalized process is still needed in order to require a clinical trial registry as mandatory.

This study showed that respondents agreed with most of proposed method at more than 90 percent to 100 percent except for few proposed methods. Those few proposed methods were related to the timeline for approval and the registration at TCTR. The

respondents provided more detailed of disagreement on the timeline that they wanted shorter timeline than proposed timeline, especially for biological drug.

Table 19: Strategy and method for the objective of efficiently control of clinical trial by Food and Drug Administration

Strategy and Method	Agree (percent)	Important (Likert scale)	Feasibility (Likert scale)	Priority (Important x Feasibility)
Strategy 1: Develop standard, procedure and criteria for evaluation	100	2.85	2.32	6.61
Method 1: Set up quality system including quality manual, SOP and criteria for evaluation.	98	2.85	2.53	7.21
Method 2: Issue the regulation that clearly identify types of investigational drug used clinical trial which are ; -drug never registered in any countries -drug already registered with new indication, new posology or new user group. -drug already registered (Phase IV)	98.1	2.63	2.54	6.68
Method 3: Issue the regulation that clearly specifies role and responsibility of involved parties, approval, monitor and revoke process.	98	2.62	2.51	6.58
Method 4: Improve the timeline for approval which are;	89	2.83	2.32	6.57

Strategy and Method	Agree (percent)	Important (Likert scale)	Feasibility (Likert scale)	Priority (Important x Feasibility)
-20 days for new protocol of pharmaceutical products -60 days for new protocol of biological products -5 days for already approved protocol.				
Method 5: Report the finished or ending of clinical trial study within specific timeline.	96	2.53	2.45	6.20
Method 6: Online submission for application	96	2.65	2.26	5.99
Method 7: Report the progress of clinical trial study within specific timeline.	92	2.49	2.40	5.98
Method 8: Provide the registered number of TCTR in the application for manufacture or importation of drug for clinical trial.	85	2.32	2.29	5.31
Method 9: Set up the consultation process for developing the clinical trial protocol	94	2.47	2.11	5.21
Method 10: Update the progress of clinical trial in Thailand clinical Trial Registry (TCTR).	89	2.31	2.12	4.90
Strategy 2: Develope safety monitoring process	98	2.77	2.15	5.96

Strategy and Method	Agree (percent)	Important (Likert scale)	Feasibility (Likert scale)	Priority (Important x Feasibility)
Method 1: Report of ADR within specific timeline as specified by Food and Drug Administration which are - Report SUSAR case within 7 days - Report all ADR case annually	91	2.66	2.42	6.44
Method 2: Online submission of ADR in clinical trial	98	2.62	2.25	5.90
Method 3: Site monitoring as GCP inspection.	94	2.56	2.10	5.38

4.2.3.3 To strengthen capacity building in related agencies in order to promote the clinical trial in Thailand.

The study showed that the respondents agreed with the proposed strategies to introduce capacity building in related aspects which could be summarized into 4 mains aspects which were people, place, knowledge and information. In addition, the study also showed that the respondents primarily focused on individual development, having more investigators who had an appropriate qualification and experience. This was not surprisingly found because it was the easiest and fundamental way to perform. The training of GCP, which was a basic training for all personals involved with clinical trial could be organized by a training session or online training. Many organizations also arranged the GCP training such as academia, sponsor, research institute or even Food and Drug Administration. At the beginning of introduce ICH GCP in Thailand, after memorandum among ministry of pubic health, ministry of education and PReMA in 2000, Food and Drug Administration organized many GCP trainings to any interested persons. Sponsor and academia later took the leading roles in providing this GCP training.

However, there was comparatively less agreement and feasibility in including the GCP in a curriculum. Some respondents suggested that it should be trained during the resident period in the hospital. As GCP was an essential requirement for all personal involved in the clinical trial, GCP should be one of the elective topics or courses in the heath care professional study or at least in the continuing study program.

Table 20: The summary opinion on strategies and method on capacity building

Strategy and Method	Agree (percent)	Important (Likert scale)	Feasibility (Likert scale)	Priority (Important x Feasibility)
Strategy 1: Increase the number of qualified investigator	98	2.72	2.22	6.04
Method 1: GCP Training	100	2.82	2.69	7.59
Method 2: Promote and support new investigator working with qualified investigator.	96	2.48	2.34	5.80
Method 3: Include GCP in the curriculum of health professional education.	84	2.42	2.30	5.57
Strategy 2: Increase the number of clinical site with good quality.	96	2.64	2.19	5.78
Method 1: Develop and support Laboratory to have a Good laboratory Practice (GLP).	96	2.75	2.21	6.08
Method 2: Support the conduct of clinical trial in Clinical trial Center.	92	2.44	2.20	5.37
Method 3: Develop the clinical trial management network in order to have the same standard and reduce management cost.	94	2.50	2.08	5.2

Strategy and Method	Agree (percent)	Important (Likert scale)	Feasibility (Likert scale)	Priority (Important x Feasibility)
Strategy 3: Develop database and network information related to clinical trial	98	2.73	2.04	5.57
Method 1: Set up the website containing information related to clinical trial	100	2.48	2.50	6.20
Method 2: Promote the utmost use of information in TCTR	92	2.47	2.37	5.85
Method 3: Promulgate and publish the list of Non-clinical laboratory in Thailand	96	2.41	2.27	5.47
Method 4: Be member of International Clinical Trials Registry Platform (ICTRP)	94	2.37	2.24	5.31
Method 5: Set the requirement of registration number of TCTR before published any information in Journal in Thailand	84	2.20	2.12	4.66
Strategy 4: Increase knowledge on research and development of drug or herbal drug	98	2.73	2.04	5.57
Method 1: Training on research and development process, data requirement for registration	98	2.62	2.45	6.42

4.2.4 Opinion on the indicator

The list of proposed indicators for assessment the function of clinical trial control system were asked without specifying for any specific strategies or methods using the likert scale of 5 to 1 as extremely agree, highly agree, agree, less agree and un agree, orderly. As show in the table 21, the respondents had the same opinions to have these indicators for monitoring the progress or development of clinical trial control system.

The lowest likert scale at 3.67 was the indicator for the number and percent of clinical trial protocol with registration number of Thai Clinical Trial Registry (TCTR). This was in accordance with the opinion on the strategy and method that methods related to Thai Clinical Trial Registry (TCTR) were unfavorable. This presented that the clinical trial registry concept was not well aware and understood. The purpose of clinical trial registry is to ensure the transparency, validity, value of scientific evidence of clinical trial including accessibility of information by all concerned parties such as patient, researcher, regulator and policy maker. Therefore, it is considered as an ethical and good practice to register at clinical trial registry. Most of registries are online based and electronically searchable. Some of registries are operated by government whereas others by non-profit organization. World health organization also provides International clinical trial registry platform (ICTRP) and network. Regulatory agency in some countries requires that clinical trial must be registered such as the United State of America (www.clinicaltrial.govs), India (www.ctri.nic.in), etc. In the other hand, the clinical trial registry is voluntary in some countries and there is even no requirement or system in some other countries. There was a study showing that trial registration was becoming an international standard for clinical research. In addition, the knowledge should be provided to support the researcher for deciding to comply with this standard. (Reveiz et al, 2007) Clinical trial registry in Thailand (www.clinicaltrials.in.th) was established by Medical Research Foundation, which is a non-profit organization, in 2009. The registry is voluntary. Up to now, there has been only 58 of clinical trial registered (Thai Clinical trial registry, 2013) which is comparable lower than 191 of the clinical trial conducted in Thailand and registered at www.clinicaltrial.govs.in 2013. There were some arguments that clinical trial could be registered at anywhere if it was openly access. There is no necessary to register in any individual countries because it was a redundant work. On the

contrary, if country has her own clinical registry, the data of all clinical trial conducted in the country will provide the overview situation and be useful for all concern partied such as researcher, patient, funder and policy maker. In order to strengthen the transparency, validity, value of scientific evidence, accessibility of information, the regulation on clinical registry in Thailand should be introduced and implemented. Currently there is no any legal frameworks directly related to the clinical trial registry. Food and Drug administration, which has a responsibility to control the manufacture or importation of investigational drug for clinical trial used in Thailand, should take a role by requiring the Thai clinical registry number in the process of approval. At the beginning, it could be voluntary until the researchers have enough knowledge and awareness of the important and useful of clinical registry, and then become a mandatory. This mechanism has been successfully implemented in India. (Pandey et al, 2013) The legislation process normally takes time to be issues and implement In addition, In the absence of legislation, medical journal editors have an important role in clinical trial registry.

Table 21: The summary opinion on proposed indicator

Indicator	Mean (Std.deviation)
Indicator group I : Standard of Ethical committee	
1.Human research acts availability	4.25 (0.99)
2.Regulation and criteria for ethical committee recognition	4.31 (0.86)
3.Number of recognized ethical committee	4.18 (0.79)
4.Number of renewal or extension of recognized ethical committee	4.14 (0.80)
Indicator group II : Efficiency and effectiveness of clinical trial control by Food and Drug administration	
5. SOP for all activities and criteria for evaluation	4.63 (0.63)
6.Number and percent of import or manufacture investigational drug application received approval from Food and Drug Administration within specific timeline	4.31(0.65)
7. Time for evaluation and approval	4.41 (0.72)
8. Number and percent of import or manufacture investigational drug application submitted online	4.00 (0.85)
9. Number and percent of clinical trial protocol with registration number of Thailand Clinical Trial Registry (TCTR)	3.67 (1.13)
10.Number and percent of import or manufacture investigational drug application, and clinical trial protocol classified by phase of trial	3.82 (0.83)

Indicator	Mean (Std.deviation)
11.Number and percent of import or manufacture investigational drug application, and clinical trial protocol classified by types of investigational drug used clinical trial which are ; -drug never registered in any countries -drug already registered with new indication, new posology or new user group. -drug already registered (Phase IV)	4.00 (0.85)
12.Performance evaluation of Food and Drug Administration officer such as - percent of import or manufacture investigational drug application -percent of inspection and safety monitoring -Number of suspension or cancellation of approval	3.92 (0.85)
13.Number of clinical trial protocol having pre-submission consultation with Food and Drug Administration	3.76 (1.06)
14. Number of clinical trial protocol which submit the progress report with in specific timeline	3.78 (1.02)
15. Number of clinical trial protocol which submit the finished or ending report within specific timeline	3.88(0.92)
16. Number of clinical trial protocol which update the progress in Thailand Clinical Trial Registry (TCTR)	3.72 (1.11)
17.Summary of Suspected unexpected serious adverse reaction (SUSAR) cases in Thailand	4.00 (0.96)
18.Percent of Adverse drug reaction occurred in the trial submitted online	3.96 (0.88)
19.Number and percent of clinical trial protocol/site which are inspected comparing with eligible protocol/site (criteria for inspection)	3.96 (0.93)
20.Number and percent of inspection whose finding complied with ICH-GCP standard and approval's condition	4.12 (0.90)
Indicator group III : Capacity building to promote a good quality clinical trial in Thailand	
21. Include GCP in the curriculum of health professional education	3.72 (1.20)
22.Increasing number of Principle Investigator and Co-Investigator every year	3.90 (0.92)

Indicator	Mean (Std.deviation)
23.Increasing number of the good quality clinical trial center	4.08 (0.85)
24.Number of Laboratory certified with GLP standard	4.22 (0.82)
25.Training on research and development of new drug and herbal drug	3.80 (0.98)
26.TCTR be a Member of International Clinical Trials Registry Platform (ICTRP) within 1014	3.80 (1.06)
28.List of the list of Non-clinical laboratory in Thailand	3.92 (0.98)
28.Specific website containing information related to clinical trial	4.20 (1.02)

All indicators were categorized into groups by the objective as:

Group I for the objective I: Standard of Ethical committee

Group II for the objective II: Efficiency and effectiveness of clinical trial control by Food and Drug administration

Group III for the objective III: Capacity building to promote a good quality clinical trial in Thailand

As shown in Table 21 all stakeholders considered that Group I indicators were comparable highly appropriate, following by group III and group II consecutively. Those group indicators with higher score were for new activities. This showed that all stakeholders had a high expectation on the progress of these objectives. Whereas opinion on group II indicator which representing the performance of Food and Drug Administration in clinical trial was lower than other. This could be interpreted into two aspects. First, the respondents did not know or understand the work of Food and Drug Administration. They may not aware of the objective, process and measures of Food and Drug Administration to ensure the quality of product, the safety of patient. Hence, they did not aware how useful of these indicators. Secondly, the activities of Food and Drug Administration had long been performed but there were no data on these indicators available. The respondents may be suspicious whether these indicators could be used. The opinion by Food and drug Administration personal was not included due to a very small sample size (only 2 persons).

The study showed that opinion from Contract Research Organization (CRO) was lower than from other stakeholders' opinion. However, it had a same trend as higher in group I indicators than group II indicators except group III indicators. This could be

interpreted that they had less understand or unaware of ethical committee and Food and Drug Administration work, or well understand or aware of ethical committee and food and Food and Drug Administration work. This could be a further study.

Table 22: The summary opinion on proposed group of indicators by stakeholders

	Opinion on appropriate of indicators (scale)		
Stakeholder	Group I indicators	Group II indicators	Group III indicators
Overall	4.22	3.93	3.99
Sponsor	4.28	4.01	4.10
Contract Research Organization (CRO)	3.48	3.41	3.74
Investigator	4.46	4.20	4.35
Ethical committee	4.68	4.22	4.06
Other	4.31	3.96	3.85

Chapter V Conclusion and Recommendation

1.Conclusion

Clinical trial control system in Thailand could be considered as formally established in B.E. 2532 by Ministry of Public health notification on importation of drug for clinical trial. At the beginning, most of clinical trials are the clinical trial phase IV which involves drug that has been registered in other countries already. Therefore, there are less concerns about safety and efficacy. Consequently the requirement for application for importation is at as minimum as necessary such as certificate of free sale, label and package insert. Later the type of clinical trial study has been changed to other phases such as phase III, II and I which drugs used in the trial are not registered anywhere in the world. The safety and efficacy of these drugs are still limited therefore, the approval for importation or manufacture of these drug as well as the approval to conduct the trial is very important. The ethical committee then becomes crucial in ensuring the safety of the subject participating in clinical trial. In order to minimize the risk that may happen to the subject participating in the trial and to improve the quality of the clinical trial study, Food and Drug Administration made the amendments in the regulation to require more documents and information such as an ethical approval certificate, investigator brochure, protocol, a quality control documents of drug, etc.

The difference between the current clinical trial control and the designed clinical control were summarized as Table 23.

Table 23 The difference between current clinical trial control and the designed clinical trial control

Current clinical trial control	Designed clinical trial control
1.No law or acts governing ethical committee	1.Human research acts which governs ethical committee
2.No law or acts specify role and	2.Human research acts and Drug acts

Current clinical trial control	Designed clinical trial control
responsibility of stakeholders involved in clinical trial.	specify role and responsibility of stakeholders related to human research and drug ,respectively.
3.Scope of application for manufacture/ importation for clinical trial -unregistered drug in Thailand	3.Scope of application for manufacture/ importation for clinical trial -unregistered drug in Thailand -registered drug for new indication, new regimen, new group of patient
4.Recognized ethical committee -ten ethical committees recognized by FDA	4.Recognized ethical committee -designated unit/organization to accredit ethical committee
5.Progress report of clinical trial to FDA -only the end of clinical trial or the final report	5.Progress report of clinical trial to FDA -annual progress report by applicant
6.Voluntary submit clinical trial in clinical trial registry including Thailand clinical trial registry	6.Mandatory to submit clinical trial in clinical trial registry including Thailand clinical trial registry

The study showed that regulatory framework for clinical trial system was considerable satisfied by all stakeholders. Some issues which received comparable lower score of agreeable and appropriate were considered as the gap for improvement. There were numbers of issues identified which could be categorized into three main aspects; Food and Drug Administration, Ethical committee and capacity building. These should be done parallel in order to support the whole system and each other. The designed strategies, method and indicator were verified by the questionnaire distributed to representatives from all stakeholders. The priority was considered based on agreeable, important and feasibility. The summary of these strategies and method classified based on responsible agency or body was presented as Table 24.

Table 24: Strategies and methods for the clinical trial control system in Thailand.

Food and Drug Administration
Strategy 1: Develop and strengthen quality system including standard, procedure and criteria for evaluation
Method 1: Set up quality system including quality manual, SOP and criteria for evaluation. Method 2: Issue the regulation that clearly identify types of investigational drug used clinical trial Method 3: Issue the regulation that clearly specifies role and responsibility of involved parties, approval, monitor and revoke process. Method 4: Improve the timeline for approval Method 5: Report the finished or ending of clinical trial study within specific timeline Method 6: Online submission for application Method 7: Report the progress of clinical trial study within specific timeline Method 8: Provide the registered number of TCTR in the application for manufacture or importation of drug for clinical trial. Method 9: Set up the consultation process for developing the clinical trial protocol Method 10: Update the progress of clinical trial in Thailand clinical Trial Registry (TCTR)
Strategy 2: Develop safety monitoring process
Method 1: Report of ADR within specific timeline as specified by Food and Drug Administration Method 2: Online submission of ADR in clinical trial Method 3: GCP inspection
Ethical committee
Strategy 1: An accreditation or recognition system
Method 1: Define or set up a specific agency responsible for accreditation or recognition Method 2: Monitor periodically every two years

Strategy 2: National standard for Ethical committee
Method 1: Each institution formally establishes an ethical committee or recognizes other institution's ethical committee complied with ICH-GCP standard. Method 2: Food and Drug administration issues the regulation on ethical committee recognition. Method 3: Thailand has Human Research Acts.
Interagency(Cooperation among all related stakeholders)
Strategy 1: Increase the number of qualified investigator
Method 1: GCP Training Method 2: Promote and support new investigator working with qualified investigator. Method 3: Include GCP in the curriculum of health professional education.
Strategy 2: Increase the number of clinical site with good quality.
Method 1: Develop and support Laboratory to have a Good laboratory Practice (GLP). Method 2: Support the conduct of clinical trial in Clinical trial Center. Method 3: Develop the clinical trial management network in order to have the same standard and reduce management cost.
Strategy 3: Develop database and network information related to clinical trial
Method 1: Set up the website containing information related to clinical trial Method 2: Promote the utmost use of information in TCTR Method 3: Promulgate and publish the list of Non-clinical laboratory in Thailand Method 4: Be member of International Clinical Trials Registry Platform (ICTRP) Method 5: Set the requirement of registration number of TCTR before published any information in Journal in Thailand
Strategy 4: Increase knowledge on research and development of drug or herbal drug
Method 1: Training on research and development process, data requirement for registration

There were many agencies involved in ethical committee aspects such as ministry of public health, national research council of Thailand, forum for ethical committees

review in Thailand and FDA. They should work and support each other in order to strengthen the ethical control system. National research council of Thailand could be the main responsible body for Human research acts whereas other agencies are the supporting agency in the areas that specifically related to them. For example, while human research act is under drafting and public hearing process, FDA could issue the regulation on the criteria for recognized ethical committee. This will assure that ethical committee which reviews clinical trial protocol has a good quality review and the subjects are protected.

As mentioned in table 23, there were strategies and methods that were cooperated among stakeholders. Some methods could be the responsible by particular agency whereas other method could be the responsible of more than one agency. For example, any stakeholders such as FDA, sponsor, investigator, contract research organization, ethical committee or academia, could organize GCP training. FDA organized many GCP trainings during 2000-2005. In order to establish the concept and principle of good clinical practice in all health professional, GCP should incorporate into curriculum of healthcare professional. The responsible agencies for each method were presented in Table 25.

Table 25 Responsible agency for strategies and methods requiring cooperation among related stakeholders

Strategy/Method	Responsible agency
Strategy 1: Increase the number of qualified investigator	
Method 1: GCP Training	All stakeholders
Method 2: Promote and support new investigator working with qualified investigator.	Sponsors, Contract research organization
Method 3: Include GCP in the curriculum of health professional education.	Academia

Strategy/Method	Responsible agency
Strategy 2: Increase the number of clinical site with good quality.	
Method 1: Develop and support Laboratory to have a Good laboratory Practice (GLP)	Ministry of Public health, Food and Drug Administration and Department of Medical sciences.
Method 2: Support the conduct of clinical trial in Clinical trial Center	Sponsors, Contract research organization, Investigator
Method 3: Develop the clinical trial management network in order to have the same standard and reduce management cost.	Contract research organization, Academia
Strategy 3: Develop database and network information related to clinical trial	
Method 1: Set up the website containing information related to clinical trial	Food and Drug Administration
Method 2: Promote the utmost use of information in TCTR	Sponsors, Contract research organization, Investigator
Method 3: Promulgate and publish the list of Non-clinical laboratory in Thailand	Food and Drug Administration
Method 4: Be member of International Clinical Trials Registry Platform (ICTRP)	Medical research foundation
Method 5: Set the requirement of registration number of TCTR before published any information in Journal in Thailand	Academia
Strategy 4: Increase knowledge on research and development of drug or herbal drug	
Method 1: Training on research and development process, data requirement for registration	Academia, Food and Drug administration, Sponsor and Contract research organization

In order to improve and strengthen the clinical trial system in Thailand, cooperation among concerned parties is the key factor for the successful.

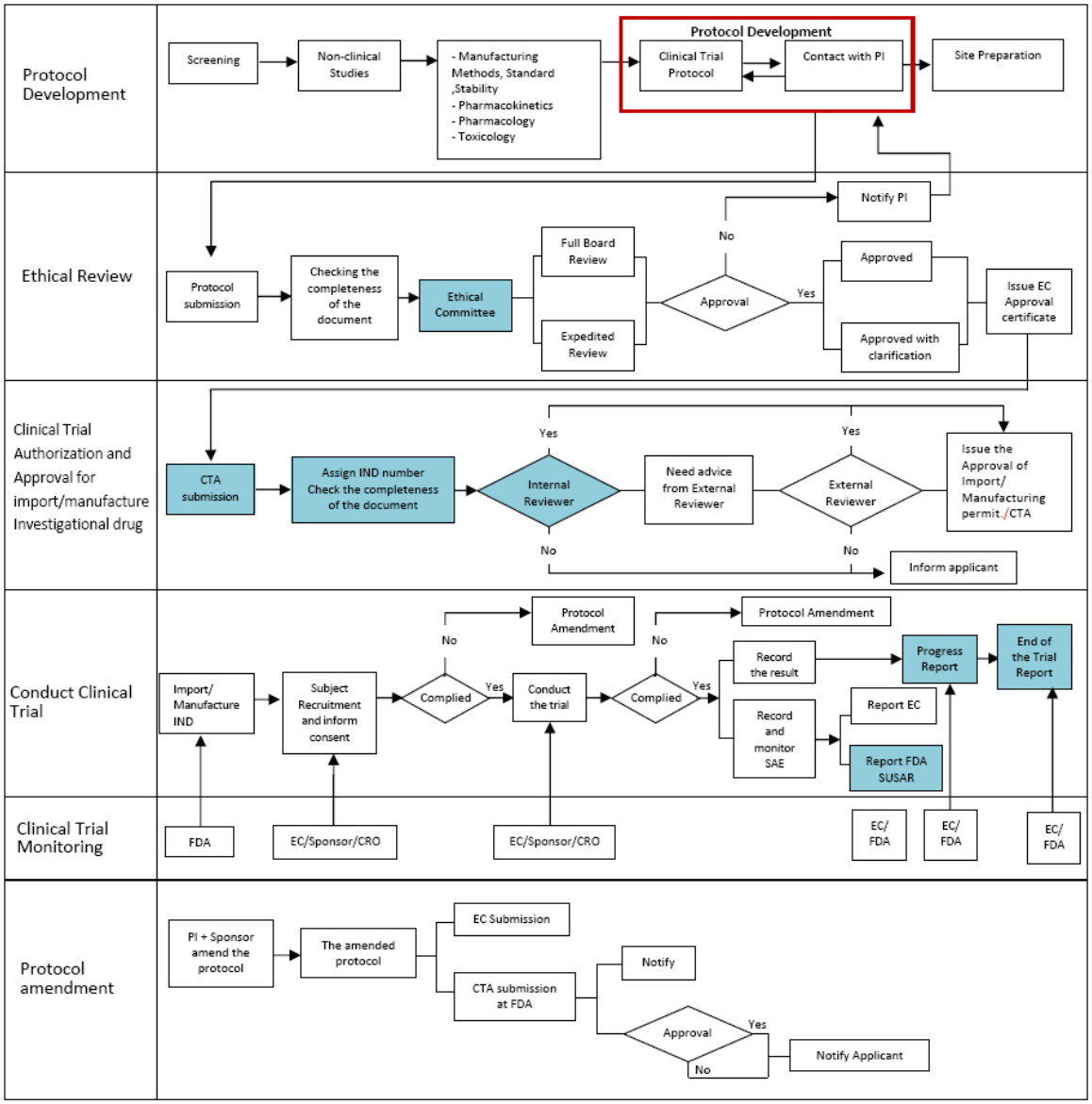

Figure 8: The diagram of identified priority process related to clinical trial

As clinical trial involved many stakeholders, the improvement of system need tremendous efforts from all stakeholders. However, sponsor, investigator and contract research organization may have their interested and priority. Therefore this study focused mainly on the process involving Food and Drug Administration and ethical committee.

The priorities of realization were the standard of ethical committee approval, Food and Drug Administration approval and report of ADR, progress and final.

2.Recommendation

The improvement of clinical trial control system is very crucial in order to ensure the right and well being of subject, the value, validity and merit of scientific data. The priority of main strategies were as follow;

1. To establish a standard for Ethical Committee including accreditation system
2. To strengthen the clinical trial approval of Thai Food and Drug Administration
3. To promote knowledge management on Research and development

The policy on issuing acts concerning the ethical committee and subject protection

should be politically commitment. The amendment of Drug acts or issuing new drug acts also need politically commitment and support from all stakeholders.

To realize the effectiveness of clinical trial control, Food and Drug Administration should:

- Improve the process of clinical trial authorization for approval manufacture or import investigational drug.
- Strengthen safety monitoring during clinical trial by facilitating the method and timeline for reporting adverse drug reaction.
- Sharing information and knowledge on the regulation, process and work of Food and Drug administration on clinical trial control.
- Taking a leading role in establish a criteria standard of ethical committee that review clinical trial protocol using investigational drug.
- To realize the standard of Ethical committee, Food and Drug Administration, taking a leading role, should :

To realize the knowledge management on Research and development, Medical Research Network of the Consortium of Thai medical school (MedResNet) should:

- Be an interagency to cooperate among stakeholders

- Disseminate and distribute all information related to research and development, conducting clinical trial in Thailand

3.Limitation

There were some limitations in this study. Firstly, the sample size of each stakeholder is quite difference. For example, there were only 5 and 2 person from Food and Drug Administration in the first and second questionnaire survey. On the other hand, the investigator and ethical committee were the majority of the respondents. In addition, this study did not include the patient as one of stakeholders. A few groups of patient advocacy could be identified but may not be the same group as advocacy group participating in clinical trial.

4.Future works

The further study is to follow up the implementation of each selected strategies and methods by related organizations involving in clinical trial. The study on perceptions of subjects in clinical trial should also be conducted.

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APPENDICES

APPENDIX A

Questionnaire: The opinion on current situation and designed system for clinical trial control system in Thailand

แบบสอบถามเรื่องการกำกับดูแลการวิจัยทางคลินิกในประเทศไทย

การศึกษาวิจัยทางคลินิกซึ่งมีผู้เข้าร่วมการศึกษาเป็นผู้ป่วยหรือเป็นผู้ที่มีสุขภาพดี มีความสำคัญเป็นอย่างมากต่อการวิจัยและการพัฒนายาใหม่เพื่อนำยามารักษา บรรเทาอาการของโรคต่างๆ นอกจากนี้เมื่อมีการนำยาใหม่ต่างๆมาเริ่มใช้ในสถานการณ์จริงๆยังต้องมีการติดตามผลการใช้ทั้งในแง่ประสิทธิภาพ ความปลอดภัย ทั้งนี้การศึกษาวิจัยทางคลินิกยังมีความเสี่ยงต่ออาสาสมัครที่เข้าร่วมในการศึกษาวิจัย ดังนั้นเพื่อไม่ให้ประชาชนที่เข้าร่วมในการศึกษาวิจัยได้รับการคุ้มครอง จึงมีความจำเป็นที่ภาครัฐจะต้องจัดตั้งและพัฒนากลไกที่จะสร้างความมั่นใจว่าประชาชนที่เข้าร่วมการศึกษาวิจัยได้รับการปกป้องคุ้มครองความปลอดภัยอย่างดี มีมาตรฐาน และมีการส่งเสริมการศึกษาวิจัยทางคลินิกในประเทศไทยที่มาตรฐานเป็นที่ยอมรับเพิ่มมากขึ้น ในอดีตขั้นตอนการศึกษาวิจัยทางคลินิกในประเทศไทยยังไม่มีมากนัก แต่ในปัจจุบันมีหลายปัจจัยที่เอื้อให้มีการศึกษาวิจัยทางคลินิกในประเทศไทยมากขึ้น เช่นสถานพยาบาลที่มีระบบการจัดการและเทคโนโลยีที่ทันสมัย บุคลากรทางการแพทย์ที่มีคุณภาพ ซึ่งจะเห็นได้จากแนวโน้มที่มีการขออนุญาตนำเข้ายาเพื่อการวิจัยทางคลินิกเพิ่มขึ้น ทั้งนี้หน่วยงานรัฐที่เกี่ยวข้องโดยตรง ณ ปัจจุบันได้แก่สำนักงานคณะกรรมการอาหารและยาซึ่งเป็นการกำกับดูแลในแง่การควบคุมการผลิตหรือนำเข้ายาเพื่อการวิจัยเท่านั้น แต่ยังมีปัจจัยหรือประเด็นอื่นอีกหลายอย่างที่เกี่ยวข้องกับการวิจัยทางคลินิกที่ยังไม่มีกฎหมาย หรือกฎระเบียบของประเทศรองรับโดยตรง หรือมีหน่วยงานหรือผู้ดูแลรับผิดชอบโดยตรงหรือเป็นทางการเช่น คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน การขึ้นทะเบียนหรือจดแจ้งการศึกษาวิจัยทางคลินิกของประเทศไทย ดังนั้นเพื่อเป็นการพัฒนาและเตรียมความพร้อมรองรับกับยุคโลกาภิวัฒน์และการเป็นประชาคมเศรษฐกิจอาเซียน จึงมีความจำเป็นที่ต้องศึกษาสถานการณ์ ณ ปัจจุบัน และวางกรอบเพื่อการพัฒนาปรับปรุงระบบการกำกับดูแลการวิจัยยาทางคลินิกในภาพรวมของประเทศไทยต่อไป

สำนักงานคณะกรรมการอาหารและยามีแนวคิดในการพัฒนาระบบการกำกับดูแลยาวิจัยทางคลินิก เพื่อให้การพัฒนาการกำกับดูแลเป็นไปอย่างเหมาะสม มีประสิทธิภาพ สามารถนำมาปฏิบัติได้จริง และไม่เป็นอุปสรรคต่อการพัฒนาการศึกษาวิจัยภายในประเทศและส่งเสริมการสร้างความรู้ของประเทศ ทั้งนี้การปรับปรุงดังกล่าวจะส่งผลกระทบต่อผู้ที่เกี่ยวข้องทุกภาคส่วนเช่นผู้วิจัย คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน ผู้สนับสนุนการวิจัย บริษัทที่รับทำการศึกษาวิจัย องค์กรที่ให้ทุนเพื่อการศึกษาวิจัย และสำนักงานคณะกรรมการอาหารและยา ดังนั้นความคิดเห็นและความคาดหวังของท่านต่อการกำกับดูแลการวิจัยทางคลินิกในประเทศไทยจึงมีความสำคัญและจำเป็นอย่างมาก ผลของการศึกษานี้จะได้นำไปเป็นข้อมูลพื้นฐานในการพัฒนา ปรับปรุงและจัดทำเป็นนโยบายในการจัดการเรื่องการศึกษาวิจัยทางคลินิกในประเทศไทยให้เหมาะสมกับสถานการณ์ที่เปลี่ยนแปลงไป เพื่อเป็นการคุ้มครองผู้เข้าร่วมในการศึกษาวิจัย และส่งเสริมพัฒนาการศึกษาวิจัยในประเทศต่อไป

คำชี้แจง

1. แบบสอบถามนี้มีวัตถุประสงค์เพื่อศึกษาสถานการณ์การกำกับดูแลการวิจัยทางคลินิก ณ ปัจจุบันและความคิดเห็นต่อการปรับปรุงแนวทางการกำกับดูแลการวิจัยทางคลินิก ทั้งนี้เฉพาะการศึกษาวิจัยทางคลินิกที่เกี่ยวข้องกับยาเท่านั้น
2. เนื้อหาในแบบสอบถามนี้ประกอบด้วยคำถาม 3 ตอน คือ
   ตอนที่ 1 ข้อมูลทั่วไปของผู้ตอบแบบสอบถาม
   ตอนที่ 2 สถานการณ์การกำกับดูแลการวิจัยทางคลินิก ณ ปัจจุบัน
   ตอนที่ 3 ความเห็นต่อการปรับปรุงแนวทางการกำกับดูแลการวิจัยทางคลินิก
3. คำตอบของท่านมีค่าอย่างยิ่ง จึงใคร่ขอความร่วมมือจากท่านในตอบคำถามตามความเป็นจริง และขอขอบพระคุณที่ท่านได้สละเวลาอันมีค่าตอบแบบสอบถามฉบับนี้
4. เมื่อตอบเสร็จแล้ว ขอท่านส่งแบบสอบถามกลับที่ นางสาวจารุณี กฤษณพันธ์ กลุ่มกำหนดมาตรฐาน สำนักยา สำนักงานคณะกรรมการอาหารและยา กระทรวงสาธารณสุข อำเภอเมือง นนทบุรี 11000 หรือ โทรสารที่ 02 5907360

ส่วนที่ 1 ข้อมูลทั่วไป

1. ปัจจุบันท่านเกี่ยวข้องกับการศึกษาวิจัยทางคลินิกในฐานะ (เลือกได้มากกว่า 1 ข้อ)
   - ☐ Sponsor เป็นระยะเวลา ..... ปี
   - ☐ Investigator เป็นระยะเวลา ..... ปี
   - ☐ Ethical Committee เป็นระยะเวลา ..... ปี
   - ☐ Contract Research Organization (CRO) เป็นระยะเวลา ..... ปี
   - ☐ Regulator (สำนักงานคณะกรรมการอาหารและยา) เป็นระยะเวลา ..... ปี
   - ☐ อื่นๆ โปรดระบุ..... เป็นระยะเวลา ..... ปี
2. สาขาวิชาชีพของท่าน
   - ☐ แพทย์
   - ☐ เภสัชกร
   - ☐ พยาบาล
   - ☐ เทคนิกการแพทย์
   - ☐ นิติกร
   - ☐ อื่นๆ โปรดระบุ.....
3. ระดับการศึกษาสูงสุด
   - ☐ ปริญญาตรี
   - ☐ ปริญญาโท
   - ☐ ปริญญาเอก
4. ท่านเคยเข้ารับการอบรมเกี่ยวกับเรื่องจริยธรรมการวิจัย หรือ การปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practice: GCP) หรือไม่ (เลือกได้มากกว่า 1 ข้อ)
   - ☐ เคยเข้ารับการอบรมเรื่องจริยธรรมการวิจัย
   - ☐ เคยเข้ารับการอบรมเรื่องการปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practice: GCP)
   - ☐ ไม่เคยเข้ารับการอบรม
   - ☐ เคยเข้ารับการอบรมเรื่องอื่นๆ โปรดระบุ.....

ส่วนที่ 2 ความเห็นต่อสถานการณ์การกำกับดูแลการวิจัยทางคลินิก ณ ปัจจุบัน โปรดใส่เครื่องหมาย √ ในช่องที่ท่านเคยมีประสบการณ์ หรือตรงกับความเห็นของท่านมากที่สุด

1. ท่านเคยมีประสบการณ์การวิจัยทางคลินิกกับยาประเภทใด และดำเนินการยื่นขออนุญาตอย่างไร โปรดระบุ

☐ ยาที่ได้รับอนุญาตทะเบียนตำรับยาในประเทศไทยแล้ว โดย

- ○ เป็นการศึกษาตามข้อบ่งใช้ที่ได้รับอนุญาตแล้ว ซึ่งได้ยื่นขออนุญาตต่อ ☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (จริยธรรมการวิจัย) ☐ สำนักงานคณะกรรมการอาหารและยา (การผลิต/นำเข้ายาเพื่อการวิจัย)
- ○ เป็นการศึกษาตามข้อบ่งใช้ใหม่ที่ยังไม่ได้รับอนุญาต ซึ่งได้ยื่นขออนุญาตต่อ ☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (จริยธรรมการวิจัย) ☐ สำนักงานคณะกรรมการอาหารและยา (การผลิต/นำเข้ายาเพื่อการวิจัย)

☐ ยาที่ยังไม่ได้รับอนุญาตทะเบียนตำรับยาในประเทศไทย

- ○ เป็นการศึกษาวิจัย Phase I ซึ่งได้ยื่นขออนุญาตต่อ ☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (จริยธรรมการวิจัย) ☐ สำนักงานคณะกรรมการอาหารและยา (การผลิต/นำเข้ายาเพื่อการวิจัย)
- ○ เป็นการศึกษาวิจัย Phase II ซึ่งได้ยื่นขออนุญาตต่อ ☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (จริยธรรมการวิจัย) ☐ สำนักงานคณะกรรมการอาหารและยา (การผลิต/นำเข้ายาเพื่อการวิจัย)
- ○ เป็นการศึกษาวิจัย Phase III ซึ่งได้ยื่นขออนุญาตต่อ ☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (จริยธรรมการวิจัย) ☐ สำนักงานคณะกรรมการอาหารและยา (การผลิต/นำเข้ายาเพื่อการวิจัย)

2. โดยทั่วไปท่านยื่นขออนุญาตจริยธรรมการวิจัยจากคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน ที่หน่วยงานใด (เลือกได้มากกว่า 1 ข้อ)

☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน กระทรวงสาธารณสุข อยู่ภายใต้การกำกับดูแลของ กรมการแพทย์ กระทรวงสาธารณสุข
☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์ กระทรวงสาธารณสุข อยู่ภายใต้การกำกับดูแลของกระทรวงสาธารณสุข
☐ คณะกรรมการกลางพิจารณาจริยธรรมการวิจัย (Central Research Ethics Committee, CREC) อยู่ภายใต้การกำกับดูแลของสภาวิจัยแห่งชาติ
☐ คณะกรรมการพิจารณาจริยธรรมของสถาบัน..... อยู่ภายใต้การกำกับดูแลของ (โปรดระบุ) .....

3. นอกจากการขออนุญาตการผลิต หรือนำเข้ายาเพื่อการวิจัยทางคลินิกที่ดำเนินการ ณ สำนักงานคณะกรรมการอาหารและยาแล้ว ท่านมีการขึ้นทะเบียน/จดแจ้งข้อมูลการศึกษาวิจัยทางคลินิกที่ท่านดำเนินการหรือไม่ (เลือกได้มากกว่า 1 ข้อ)

☐ มี แจ้งที่ International Clinical Trials Registry Platform (WHO ICTRP)
☐ มี แจ้งที่ www.Clinicaltrials.gov
☐ มี แจ้งที่ Thai Clinical Registry (TCRT)
☐ มี แจ้งที่ โปรดระบุ.....
☐ ไม่มี

4. ความคิดเห็นของท่านต่อการดำเนินการที่เกี่ยวข้องกับการศึกษาวิจัยทางคลินิก โปรดเลือก √ ในช่องที่ตรงกับความเห็นของท่านมากที่สุด

	เหมาะสมมากที่สุด	เหมาะสมมาก	ปานกลาง	เหมาะสมน้อย	ไม่เหมาะสม
4.1 องค์ประกอบของคณะกรรมการพิจารณาจริยธรรมการวิจัยในมนุษย์ตามที่กำหนดใน ICH GCP guideline มีความเหมาะสมหรือไม่					
4.2 คู่มือขั้นตอนปฏิบัติงานของ**คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน**ที่ท่านเคยมีประสบการณ์มีความเหมาะสมหรือไม่					
4.3 ขั้นตอนการดำเนินการพิจารณาของ**คณะกรรมการพิจารณาจริยธรรมในคน**ที่ท่านเคยมีประสบการณ์มีความเหมาะสมหรือไม่					
4.4 ระบบรายงานเหตุการไม่พึงประสงค์ที่เกิดระหว่างการศึกษาวิจัยทางคลินิกต่อ**คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน**เหมาะสมหรือไม่					
4.5 การรายงานเฉพาะอาการไม่พึงประสงค์จากยาชนิดร้ายแรงที่ไม่ได้คาดคิดมาก่อนที่พบในประเทศไทย(Suspected Unsuspected Serious Adverse Reactions: SUSAR)ต่อ**สำนักงานคณะกรรมการอาหารและยา**เหมาะสมหรือไม่					
4.6 การรายงานความก้าวหน้าของโครงการวิจัยตามระยะเวลาที่**คณะกรรมการพิจารณาจริยธรรมในคน**(ที่ท่านเคยมีประสบการณ์) กำหนดมีความเหมาะสมหรือไม่					
4.7 การรายงานความก้าวหน้าของโครงการวิจัยตามระยะเวลาที่**สำนักงานคณะกรรมการอาหารและยา**(ที่ท่านเคยมีประสบการณ์) กำหนดมีความเหมาะสมหรือไม่					

	เหมาะสมมากที่สุด	เหมาะสมมาก	ปานกลาง	เหมาะสมน้อย	ไม่เหมาะสม
4.8 ระบบการให้คำปรึกษาและแนะนำในการจัดทำและปรับปรุงโครงร่างการศึกษาวิจัยโดย**คณะกรรมการพิจารณาจริยธรรมในคน** (ที่ท่านมีประสบการณ์) มีความเหมาะสมหรือไม่					
4.9 ระบบการให้คำปรึกษาและแนะนำในการจัดทำและปรับปรุงโครงร่างการศึกษาวิจัยโดย**สำนักงานคณะกรรมการอาหารและยา** (ที่ท่านมีประสบการณ์) มีความเหมาะสมหรือไม่					
	ปีละครั้ง	จัดเป็นประจำตามระยะเวลาที่กำหนด (2-3ปี/ครั้ง)	ไม่แน่นอน	ไม่ได้จัดอบรม แต่อนุญาตให้ไปรับอบรมจากหน่วยงานอื่นๆ	ไม่มีนโยบายสนับสนุนการอบรมที่ชัดเจน
4.10 หน่วยงานของท่านมีการจัดอบรมเกี่ยวกับจริยธรรมการวิจัย หรือ การปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practice: GCP) หรือไม่					
	ชัดเจนมากที่สุด	ชัดเจนมาก	ปานกลาง	ชัดเจนน้อย	ไม่ชัดเจน
4.11 เอกสารคำแนะนำสำหรับยื่นขออนุญาตจาก**คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน**มีความชัดเจนเพียงพอหรือไม่					
4.12 มีการกำหนดระยะเวลาการพิจารณาของ**คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน**ในแต่ละขั้นตอนตั้งแต่ต้นจนกระทั่งแล้วเสร็จชัดเจนหรือไม่					
4.13 เอกสารคำแนะนำสำหรับยื่นขออนุญาตผลิต/นำเข้ายาเพื่อการวิจัยจาก**สำนักงานคณะกรรมการอาหารและยา**มีความชัดเจนเพียงพอหรือไม่					
4.14มีการกำหนดระยะเวลาในการพิจารณาในแต่ละขั้นตอนตั้งแต่ต้นจนกระทั่งแล้วเสร็จของ**สำนักงานคณะกรรมการอาหารและยา**ชัดเจนหรือไม่					
4.15 งานวิจัยที่ท่านมีส่วนเกี่ยวข้องมีการกำหนดบทบาทและหน้าที่ของผู้ที่เกี่ยวข้องชัดเจนดีหรือไม่					

	ดีมาก	ดี	ปานกลาง	พอใช้	ไม่ดี
4.16ท่านมีความรู้ ความเข้าใจเกี่ยวกับ Good Clinical Practice (GCP) ในระดับใด					
4.17 ในบทบาทที่ท่านเป็นส่วนหนึ่งของการวิจัยทางคลินิก ท่านมีการปฏิบัติตาม Good Clinical Practice (GCP) ในระดับใด					

5. ท่านมีประสบการณ์ถูกตรวจติดตามการปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practices-GCP Inspection/Audit) โดยหน่วยงานใด (เลือกได้มากกว่า 1 ข้อ)
   - ☐ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน กระทรวงสาธารณสุข
   - ☐คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์ กระทรวงสาธารณสุข
   - ☐ คณะกรรมการกลางพิจารณาจริยธรรมการวิจัย (Central Research Ethics Committee, CREC)
   - ☐ คณะกรรมการพิจารณาจริยธรรมของสถาบัน.....
   - ☐ สำนักงานคณะกรรมการอาหารและยา
   - ☐ ผู้ให้ทุนวิจัย (Sponsor)
   - ☐ หน่วยงานรับจ้างทำวิจัย (Contract Research Organization-CRO)
   - ☐ อื่นๆ โปรดระบุ.....
   - ☐ ไม่เคยถูกตรวจติดตาม

ส่วนที่ 3 ความเห็นต่อการปรับปรุงแนวทางการกำกับดูแลการวิจัยทางคลินิก โปรดทำเครื่องหมาย √ ในช่องที่ตรงกับความเห็นของท่านมากที่สุด
การศึกษาวิจัยทางคลินิกเกี่ยวข้องกับประเด็นที่สำคัญ 2 ส่วนคือจริยธรรมของการวิจัยในคนและผลิตภัณฑ์ที่ใช้ในการศึกษาวิจัย ดังนั้นเพื่อเป็นการคุ้มครองผู้เข้าร่วมในการศึกษาวิจัยทางคลินิก (Subjects) จึงต้องมีมาตรการในการกำกับดูแลทั้ง 2 ส่วนอย่างเหมาะสม ทั้งนี้โดยทั่วไปการกำกับดูแลด้านจริยธรรมการวิจัยในคนจะเป็นหน้าที่ความรับผิดชอบของคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน และการกำกับดูแลด้านผลิตภัณฑ์ที่ใช้ในการศึกษาวิจัยซึ่งในที่นี้คือยา จะเป็นหน้าที่ความรับผิดชอบของสำนักงานคณะกรรมการอาหารและยา ทั้งนี้เพื่อเป็นการปรับปรุงแนวทางการกำกับดูแลการวิจัยทางคลินิกในอนาคตให้มีความเหมาะสมมากยิ่งขึ้น ความคิดเห็นของท่านจะเป็นประโยชน์อย่างมากในการปรับปรุงดังกล่าว

1. ความเห็นของท่านต่อการดำเนินการที่เกี่ยวข้องกับการศึกษาวิจัยทางคลินิกในอนาคต

	ปัจจุบัน	เห็นด้วย	ไม่เห็นด้วย	ข้อเสนอแนะ
1.1การขออนุญาตการผลิตหรือนำสั่งยาเพื่อการวิจัยทางคลินิกต่อสำนักงานคณะกรรมการอาหารและยา ให้ยื่นขออนุญาตเฉพาะ -ยาที่ยังไม่ได้รับอนุญาตทะเบียนตำรับยาในประเทศไทยและ -ยาที่ได้รับอนุญาตทะเบียนตำรับยาในประเทศไทยแล้วแต่ต้องการศึกษาข้อบ่งใช้ ขนาดการใช้ยา หรือกลุ่มผู้ใช้ยาใหม่	กำหนดให้ยื่นขอเฉพาะยาที่ได้รับการยกเว้นไม่ต้องขึ้นทะเบียนตำรับยา			
1.2 ประเทศไทยควรมีกฎหมายที่ระบุบทบาท หน้าที่ความรับผิดชอบของผู้ที่เกี่ยวข้อง การขออนุญาตและการออกใบอนุญาต พนักงานเจ้าหน้าที่ การตรวจสอบ การพักใช้และการเพิกถอนใบอนุญาต ข้อบังคับและบทกำหนดโทษ **เกี่ยวกับการศึกษาวิจัยที่ใช้ยาที่ชัดเจน**	ยังไม่มีกฎระเบียบชัดเจนเกี่ยวกับการอนุญาตการศึกษาวิจัยที่ใช้ยา			
1.3 ประเทศไทยควรมีกฎหมายที่ระบุบทบาท หน้าที่ความรับผิดชอบองค์ประกอบ การดำเนินการ การตรวจสอบ ข้อบังคับ และบทกำหนดโทษ **เกี่ยวกับคณะกรรมการพิจารณาจริยธรรมในคนที่ชัดเจน**	ไม่มีกฎหมายเฉพาะ			

	ปัจจุบัน	เห็นด้วย	ไม่เห็นด้วย	ข้อเสนอแนะ
1.4 การยื่นขออนุญาตผลิตหรือนำสั่งยาจากสำนักงานคณะกรรมการอาหารและยา ต้องแนบหลักฐานได้แก่ 1. ฉลากยาทุกขนาดบรรจุ (ภาษาไทย หรือ ภาษาอังกฤษ) 2. เอกสารกำกับยา (สำหรับยาที่ขึ้นทะเบียนตำรับยาแล้ว) 3. เอกสารคู่มือผู้วิจัย (Investigator Brochure) (สำหรับยาที่ยังไม่ได้ขึ้นทะเบียน) 4. เอกสารแนะนำอาสาสมัคร (Patient Information Sheet) (ภาษาไทย) 5. สรุปย่อโครงการวิจัย (ภาษาไทย) 6. รายละเอียดโครงการวิจัย ฉบับสมบูรณ์ (ภาษาไทย หรือ ภาษาอังกฤษ) 7. เอกสารควบคุมคุณภาพและการผลิตยา -ไม่จำเป็นต้องยื่นหนังสืออนุญาตจากคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน แต่จะเริ่มทำการศึกษาวิจัยได้เมื่อได้รับอนุญาตจากคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนของสถาบันแล้วเท่านั้น	การยื่นขออนุญาตผลิตหรือนำสั่งยาจากสำนักงานคณะกรรมการอาหารและยา ต้องแนบหลักฐานได้แก่ 1.ฉลากยาทุกขนาดบรรจุ (ภาษาไทย หรือ ภาษาอังกฤษ) 2.เอกสารกำกับยา (สำหรับยาที่ขึ้นทะเบียนตำรับยาแล้ว) 3.เอกสารคู่มือผู้วิจัย (Investigator Brochure) (สำหรับยาที่ยังไม่ได้ขึ้นทะเบียน) 4.เอกสารแนะนำอาสาสมัคร (Patient Information Sheet) (ภาษาไทย) 5.สรุปย่อโครงการวิจัย (ภาษาไทย) 6.รายละเอียดโครงการวิจัย ฉบับสมบูรณ์ (ภาษาไทย หรือ ภาษาอังกฤษ) 7.เอกสารควบคุมคุณภาพและการผลิตยา 8.เอกสารอนุมัติให้ทำการวิจัยจากคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (Institutional Review Board: IRB หรือ Independent Ethics			

	ปัจจุบัน	เห็นด้วย	ไม่เห็นด้วย	ข้อเสนอแนะ
	Committee: IEC) ที่สำนักงานคณะกรรมการอาหารและยายอมรับ			
1.5 ประเทศไทยควรมีการประกาศให้การปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practices) เป็นไปตามตามแนวทาง ICH-GCP และให้มีผลบังคับใช้อย่างเป็นทางการ	เป็นเพียงความร่วมมือระหว่างกระทรวงสาธารณสุข ทบวงมหาวิทยาลัย (ในขณะนั้น) และสมาคมผู้ผลิตและวิจัยเภสัชภัณฑ์ ว่าจะดำเนินการศึกษาวิจัยให้เป็นไปตามแนวทางการปฏิบัติการวิจัยทางคลินิกที่ดี(Good Clinical Practice: GCP)			
1.6 ประเทศไทยควรมีหน่วยงานเฉพาะซึ่งมีหน้าที่ดำเนินการรับรองหรือยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน	ไม่มีหน่วยงานเฉพาะ			
1.7 การดำเนินงานของ**คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน**ได้รับการรับรองระบบคุณภาพ	มีระบบคุณภาพภายในขององค์กร			
1.8 การดำเนินงานในการกำกับดูแลการศึกษาวิจัยทางคลินิกของ**สำนักงานคณะกรรมการอาหารและยา**ได้รับการรับรองระบบคุณภาพ	มีระบบคุณภาพภายในขององค์กร			
1.9ประเทศไทยควรมีระบบที่กำหนดให้**ผู้วิจัย**ต้องรายงานอาการไม่พึงประสงค์ที่เกิดระหว่างการศึกษาวิจัยทางคลินิกต่อ**คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน**	ผู้วิจัยเป็นผู้รายงานอาการไม่พึงประสงค์ต่อคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน			
1.10 ประเทศไทยควรมีระบบที่กำหนดให้**ผู้รับอนุญาตผลิตหรือนำสั่ง**ฯต้องรายงานอาการไม่พึงประสงค์ที่เกิดระหว่างการศึกษาวิจัยทาง	ผู้รับอนุญาตผลิตหรือนำสั่งฯเป็นผู้รายงานอาการไม่พึงประสงค์ต่อ			

	ปัจจุบัน	เห็นด้วย	ไม่เห็นด้วย	ข้อเสนอแนะ
คลินิกต่อ**สำนักงานคณะกรรมการอาหารและยา**	สำนักงานคณะกรรมการอาหารและยาแบบเร่งด่วนและแบบประจำปี			
1.11 ประเทศไทยควรมีระบบรายงานความก้าวหน้าของโครงการวิจัยตามระยะเวลาที่**คณะกรรมการพิจารณาจริยธรรมในคน**กำหนด	ผู้วิจัยส่งรายงานความก้าวหน้าตามระยะเวลาที่คณะกรรมการพิจารณาจริยธรรมการวิจัยในคนกำหนด			
1.12 ประเทศไทยควรมีระบบรายงานความก้าวหน้าของโครงการวิจัยตามระยะเวลาที่**สำนักงานคณะกรรมการอาหารและยา**กำหนด เช่น รายงานประจำปี	ผู้รับอนุญาตผลิตหรือนำเข้าฯส่งรายงานสรุปเมื่อสิ้นสุดหรือยุติโครงการวิจัยเท่านั้น			
1.13 **สำนักงานคณะกรรมการอาหารและยา**ควรมีระบบการให้คำปรึกษาหรือแนะนำในการจัดทำและปรับปรุงโครงร่างการศึกษาวิจัย	ไม่มีระบบหรือขั้นตอนการดำเนินงานที่ชัดเจนในการให้คำปรึกษาหรือแนะนำ			
1.14 ประเทศไทยควรระบบที่บังคับให้การศึกษาวิจัยทางคลินิกทุกประเภทต้องขึ้นทะเบียนหรือจดแจ้ง (Thailand Clinical Trial registry)	การขึ้นทะเบียน Thailand Clinical Trail Registry ของเครือข่ายวิจัยกลุ่มสถาบันการแพทยศาสตร์แห่งประเทศไทย เป็นแบบสมัครใจ			

2. ท่านคิดว่าหน่วยงานใดควรเป็นผู้รับผิดชอบดำเนินการเกี่ยวกับกฎหมายกำกับดูแลจริยธรรมการวิจัยในคน

☐ กระทรวงสาธารณสุข

☐ สภาวิจัยแห่งชาติ

☐ อื่นๆ โปรดระบุ.....

3. ท่านคิดว่าหน่วยงานใดควรเป็นผู้รับผิดชอบดำเนินการประกาศให้การปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practices) ตามแนวทาง ICH-GCP มีผลบังคับใช้อย่างเป็นทางการ

☐ กระทรวงสาธารณสุข

☐ สภาวิจัยแห่งชาติ

☐ แพทยสภา

☐ อื่นๆ โปรดระบุ.....

4. ในกรณีที่ประเทศไทยมีระบบการขึ้นทะเบียนการศึกษาวิจัยทางคลินิก (Thailand Clinical Trial Registry) ท่านคิดว่าหน่วยงานใดควรรับผิดชอบในการขึ้นทะเบียนการวิจัยทางคลินิก

☐ กระทรวงสาธารณสุข

☐ สภาวิจัยแห่งชาติ

☐ เครือข่ายวิจัยกลุ่มสถาบันการแพทยศาสตร์แห่งประเทศไทย

☐ อื่นๆ โปรดระบุ.....

ขอขอบคุณทุกท่านที่ให้ความอนุเคราะห์ตอบแบบสอบถามฉบับนี้

APPENDIX B

Questionnaire: The opinion on development clinical trial control in Thailand

แบบสอบถามเรื่องแนวทางในการปรับปรุงการกำกับดูแลการวิจัยทางคลินิก

แบบสอบถามฉบับนี้จัดทำขึ้นเพื่อศึกษาแนวทางในการพัฒนาระบบการกำกับดูแลยาวิจัยทางคลินิก เพื่อเป็นประโยชน์ในการปรับปรุงและพัฒนาการกำกับดูแลให้เป็นไปอย่างเหมาะสม มีประสิทธิภาพ สามารถนำมาปฏิบัติได้จริง และไม่เป็นอุปสรรคต่อการพัฒนาการศึกษาวิจัยภายในประเทศและส่งเสริมการสร้างความรู้ของประเทศ ผลของการศึกษานี้จะได้นำไปเป็นข้อมูลพื้นฐานในการพัฒนา ปรับปรุงและจัดทำเป็นแนวทางในการจัดการเรื่องการศึกษาวิจัยทางคลินิกในประเทศไทยให้เหมาะสมกับสถานการณ์ที่เปลี่ยนแปลงไปเพื่อเป็นการคุ้มครองผู้เข้าร่วมในการศึกษาวิจัย และส่งเสริมพัฒนาการศึกษาวิจัยในประเทศต่อไป

คำชี้แจง

เนื้อหาในแบบสอบถามนี้ประกอบด้วยคำถาม 2 ตอน คือ

ส่วนที่ 1 ข้อมูลทั่วไปของผู้ตอบแบบสอบถาม

ส่วนที่ 2 ความเห็นต่อแนวทางการปรับปรุง พัฒนาการกำกับดูแลยาวิจัยทางคลินิก

การสอบถามนี้มีวัตถุประสงค์เพื่อนำข้อมูลมาใช้ในการพัฒนา ปรับปรุงและจัดทำข้อเสนอในการจัดการเรื่องการศึกษาวิจัยทางคลินิกในประเทศไทยให้เหมาะสมกับสถานการณ์ที่เปลี่ยนแปลงไปเพื่อเป็นการคุ้มครองผู้เข้าร่วมในการศึกษาวิจัย และส่งเสริมพัฒนาการศึกษาวิจัยในประเทศต่อไป

ในการตอบแบบสอบถามนี้ ท่านไม่ต้องระบุชื่อของท่านแต่อย่างใด ผู้ศึกษาจะเก็บแบบสอบถามนี้ไว้เป็นความลับ และจะเสนอเฉพาะข้อมูลจากการประมวลผลเท่านั้น ซึ่งผลจากความร่วมมือของท่านจะเป็นประโยชน์อย่างยิ่งต่อการศึกษาในครั้งนี้

ขอขอบพระคุณท่านที่กรุณาสละเวลาในการตอบแบบสอบถามครั้งนี้

กรุณาส่งแบบสอบถามที่โต๊ะลงทะเบียน หน้าห้องประชุม

โปรดทำเครื่องหมาย ✓ ลงในช่อง ☐ หรือกรอกข้อมูลในช่องว่างตามความคิดเห็นของท่าน

ส่วนที่ 1 ข้อมูลทั่วไป

1. ปัจจุบันท่านเกี่ยวข้องกับการศึกษาวิจัยทางคลินิกในฐานะ (เลือกได้มากกว่า 1 ข้อ)
   - ☐ 1) องค์กรที่ให้ทุนเพื่อการศึกษาวิจัย (Sponsor)
   - ☐ 2) ผู้วิจัย (Investigator)
   - ☐ 3) คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน (Ethical Committee)
   - ☐ 4) บริษัทที่รับทำการศึกษาวิจัย (CRO)
   - ☐ 5) เจ้าหน้าที่สำนักงานคณะกรรมการอาหารและยา
   - ☐ อื่นๆ โปรดระบุ.....
2. สาขาวิชาชีพของท่าน
   - ☐ 1) แพทย์
   - ☐ 2) เภสัชกร
   - ☐ 3) พยาบาล
   - ☐ 4) เทคนิกการแพทย์
   - ☐ 5) อื่นๆ โปรดระบุ.....
3. ระดับการศึกษาสูงสุด
   - ☐ 1)ปริญญาตรี
   - ☐ 2)ปริญญาโท
   - ☐ 3)ปริญญาเอก
4. ระยะเวลาที่ปฏิบัติงานที่เกี่ยวข้องกับการศึกษาวิจัยทางคลินิก
   - ☐ 1) 5 ปีหรือต่ำกว่า
   - ☐ 2) มากกว่า 5 ปีขึ้นไป- 10 ปี
   - ☐ 3) มากกว่า 10 ปีขึ้นไป- 15 ปี
   - ☐ 4) มากกว่า 15 ปีขึ้นไป- 20 ปี)
   - ☐ 5) มากกว่า 20 ปีขึ้นไป- 25 ปี
   - ☐ 6) มากกว่า 25 ปีขึ้นไป

ส่วนที่ 2 ความเห็นต่อแนวทางการปรับปรุง พัฒนาการกำกับดูแลยาวิจัยทางคลินิก

1. การปรับปรุง พัฒนาการกำกับดูแลยาวิจัยทางคลินิกควรมีวัตถุประสงค์เพื่อ

วัตถุประสงค์	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
1.ให้มีการกำกับดูแลคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนของประเทศไทยที่มีมาตรฐาน									
2.ให้การกำกับดูแลยาวิจัยทางคลินิกของสำนักงานคณะกรรมการอาหารและยามีประสิทธิภาพ									
3.ให้มีการพัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้องในการสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย									
4. ข้อเสนอแนะอื่นๆ									

2. กลยุทธ์เพื่อให้บรรลุวัตถุประสงค์

กลยุทธ์	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
วัตถุประสงค์ที่ 1 ให้มีการกำกับดูแลคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนของประเทศไทยที่มีมาตรฐาน									
1.คณะกรรมการพิจารณาจริยธรรมการวิจัยในคนมีมาตรฐานเดียวกันทั้งประเทศตามแนวทาง ICH-GCP									

กลยุทธ์	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
2.มีการรับรองหรือยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน									
3.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 2 ให้การกำกับดูแลยาวิจัยทางคลินิกของสำนักงานคณะกรรมการอาหารและยามีประสิทธิภาพ									
1.พัฒนามาตรฐาน ขั้นตอนการปฏิบัติงาน และการพิจารณา									
2.พัฒนาขั้นตอนการติดตามความปลอดภัย									
3.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 3 ให้มีการพัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้อง เพื่อสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย									
1.เพิ่มจำนวนผู้วิจัยทางคลินิกที่มีความรู้ ความสามารถในการศึกษาวิจัยทางคลินิกที่มีคุณภาพ									
2.เพิ่มจำนวนศูนย์การศึกษาวิจัยทางคลินิกที่มีคุณภาพ									
3.พัฒนาความรู้เกี่ยวกับขั้นตอนการพัฒนายาใหม่หรือยาพัฒนาจากสมุนไพร									
4.พัฒนาฐานข้อมูลและการเชื่อมโยงของข้อมูลต่างๆ									
5.ข้อเสนอแนะอื่นๆ									

3. กลวิธีการดำเนินการ

กลวิธี	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
วัตถุประสงค์ที่ 1 ให้มีการกำกับดูแลคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนของประเทศไทยที่มีมาตรฐาน									
กลยุทธ์ที่ 1.คณะกรรมการพิจารณาจริยธรรมการวิจัยในคนมีมาตรฐานเดียวกันทั้งประเทศตามแนวทาง ICH-GCP									
1.ระดับประเทศ มีพระราชบัญญัติการวิจัยในคน									
2.ระดับองค์กร อย.มีระเบียบ กฎเกณฑ์การยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนโดยกำหนด -คุณสมบัติ องค์ประกอบ -การดำเนินการ -การตรวจติดตามโดย อย.									
3.ระดับองค์กร สถาบันหรือศูนย์ศึกษาวิจัยทางคลินิกมีระเบียบในการจัดตั้งหรือยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยที่มีมาตรฐานเป็นไปตาม ICH-GCP									
4.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 1 ให้มีการกำกับดูแลคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนของประเทศไทยที่มีมาตรฐาน									
กลยุทธ์ที่ 2 การรับรองหรือยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน									
1.มีหน่วยงานเฉพาะซึ่งมีหน้าที่ดำเนินการรับรองหรือยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยในคน									
2.มีการตรวจติดตามทุก 2 ปี									
3.ข้อเสนอแนะอื่นๆ									

กลวิธี	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
วัตถุประสงค์ที่ 2 ให้การกำกับดูแลยาวิจัยทางคลินิกของสำนักงานคณะกรรมการอาหารและยามีประสิทธิภาพ									
กลยุทธ์ที่ 1 พัฒนามาตรฐาน ขั้นตอนการปฏิบัติงาน และการพิจารณา									
1. จัดทำระบบมาตรฐานการดำเนินการ เช่นคู่มือคุณภาพ ขั้นตอนการปฏิบัติงาน เกณฑ์การพิจารณา									
2.ปรับปรุงระยะเวลาในการดำเนินการ -การพิจารณาโครงการใหม่ ภายใน 20 วันทำการ สำหรับยาเคมี และ 60 วันทำการสำหรับยาชีววัตถุ -การพิจารณาโครงการที่เคยอนุญาตแล้ว ภายใน 5 วันทำการ									
3.พัฒนาการยื่นขออนุญาตผ่านทางระบบ online submission									
4.กำหนดให้แจ้งเลขที่ของ Thailand Clinical Trial Registry ในขั้นตอนการยื่นขออนุญาตผลิตหรือนำเข้ายาเพื่อการวิจัยทางคลินิก									
5.ออกระเบียบ กฎเกณฑ์ที่ระบุประเภทของยาที่ผลิตหรือนำเข้าเพื่อการศึกษาวิจัยทางคลินิกที่ชัดเจน -ยาที่ยังไม่ได้รับขึ้นทะเบียนที่ประเทศใดมาก่อน -ยาที่ได้รับขึ้นทะเบียนแล้ว แต่มีการเปลี่ยนแปลงข้อบ่งใช้ ขนาดและวิธีใช้ยา กลุ่มผู้ใช้ยา -ยาที่ได้รับการขึ้นทะเบียนแล้ว (Phase IV)									
6.ออกระเบียบ กฎเกณฑ์ ที่ระบุหน้าที่ความรับผิดชอบของผู้ที่เกี่ยวข้อง การขออนุญาต พนักงานเจ้าหน้าที่ การตรวจติดตาม การพักใช้ การเพิกถอนการอนุญาตที่ชัดเจน									

กลวิธี	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
7.มีระบบให้คำปรึกษาในการพัฒนาจัดทำโครงการศึกษาวิจัย									
8.ให้ผู้รับอนุญาตรายงานความคืบหน้าของโครงการตามกำหนดเวลา									
9.ให้ผู้รับอนุญาตรายงานการจบโครงการวิจัยตามกำหนดเวลา									
10.กำหนดให้โครงการวิจัยมีการบันทึกความคืบหน้าของโครงการในฐานข้อมูล Thailand Clinical Trial Registry									
11.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 2 ให้การกำกับดูแลยาวิจัยทางคลินิกของสำนักงานคณะกรรมการอาหารและยามีประสิทธิภาพ									
กลยุทธ์ที่ 2.พัฒนาขั้นตอนการติดตามความปลอดภัย									
1.มีการรายงานอาการไม่พึงประสงค์ที่เกิดจากการใช้ยาวิจัยทางคลินิกภายในเวลาตามประกาศฯของ อย. -รายงาน SUSAR ภายใน 7 วัน -รายงาน ADR ประจำปี									
2.พัฒนาการรายงานอาการไม่พึงประสงค์ผ่านทาง online submission									
3.มีการตรวจติดตามการดำเนินการของโครงการ ณ สถานที่วิจัย									
4.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 3 ให้มีการพัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้อง เพื่อสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย									
กลยุทธ์ที่ 1.เพิ่มจำนวนผู้วิจัยทางคลินิกที่ความรู้ ความสามารถในการทำการศึกษาวิจัยทางคลินิกที่มีคุณภาพ									
1.มีการอบรมความรู้ที่จำเป็นต่อการเป็นผู้วิจัยทางคลินิกที่ดีเช่น ICH-GCP อย่างต่อเนื่อง									

กลวิธี	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
2.จัดเรื่อง GCPเป็นเนื้อหาหนึ่งในหลักสูตรปริญญาตรีของสาขาแพทยศาสตร์ ทันตแพทย์ศาสตร์ เภสัชศาสตร์ พยาบาลศาสตร์									
3.สนับสนุนให้ผู้วิจัยใหม่เป็นผู้วิจัยร่วมกับผู้วิจัยที่มีประสบการณ์มาก									
4.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 3 ให้มีการพัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้อง เพื่อสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย									
กลยุทธ์ที่ 2 เพิ่มจำนวนศูนย์การศึกษาวิจัยทางคลินิกที่มีคุณภาพ									
1.ส่งเสริมให้การศึกษาวิจัยทางคลินิกดำเนินการภายใต้ศูนย์การศึกษาวิจัย (Clinical trail Center)									
2.พัฒนาเครือข่ายในการบริหารจัดการเพื่อให้มีมาตรฐานเดียวกันและลดภาระด้านการจัดการ									
3.พัฒนา ยกระดับห้องปฏิบัติการให้มีมาตรฐานตาม Good Laboratory Practice (GLP)									
4.ข้อเสนอแนะอื่นๆ									
วัตถุประสงค์ที่ 3 ให้มีการพัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้อง เพื่อสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย									
กลยุทธ์ที่ 3 พัฒนาความรู้เกี่ยวกับขั้นตอนการพัฒนายาใหม่หรือยาพัฒนาจากสมุนไพร									
1ไม่การอบรมเรื่อง -การการพัฒนายา -ข้อมูลที่จำเป็นต่อการขึ้นทะเบียนทางด้านคุณภาพ พิษวิทยา เภสัชวิทยา ประสิทธิภาพ และความปลอดภัย									
2.ข้อเสนอแนะอื่นๆ									

กลวิธี	ความเห็น		ระดับความสำคัญ			ระดับความเป็นไปได้ในการนำมาปฏิบัติ			ความเห็น/ข้อเสนอแนะเพิ่มเติม
	เห็นด้วย	ไม่เห็นด้วย	มาก	ปานกลาง	น้อย	มาก	ปานกลาง	น้อย	
วัตถุประสงค์ที่ 3 พัฒนาศักยภาพของหน่วยงานที่เกี่ยวข้อง เพื่อสนับสนุนการศึกษาวิจัยทางคลินิกในประเทศไทย									
กลยุทธ์ที่ 4 พัฒนาฐานข้อมูลและการเชื่อมโยงของข้อมูลต่างๆ									
1.Thailand Clinical Trial Registry เป็นสมาชิก International Clinical Trials Registry Platform (ICTRP) ขององค์การอนามัยโลก									
2.รวบรวมรายชื่อสถาบันหรือสถานที่ศึกษาวิจัยทางด้าน Non-clinic ทั้งหมดในประเทศไทย									
3.จัดทำเว็บไซต์เพื่อเผยแพร่ข้อมูลที่เกี่ยวข้องกับการวิจัยยาทางคลินิก									
4.ส่งเสริมการใช้ประโยชน์จากฐานข้อมูลใน Thailand Clinical Trial Registry									
5.กำหนดให้การเผยแพร่ข้อมูลการศึกษาวิจัยทางคลินิกในวารสารวิชาการในประเทศไทยต้องมีเลขที่ของ Thailand Clinical Trial Registry									
6.ข้อเสนอแนะอื่นๆ									

4. ตัวชี้วัด

ตัวชี้วัด	ความเห็น				
	เห็นด้วยอย่างยิ่ง	เห็นด้วยมาก	เห็นด้วย	เห็นด้วยน้อย	ไม่เห็นด้วย
1.มีพระราชบัญญัติการวิจัยในคน					
2.มีประกาศ กฎเกณฑ์การยอมรับคณะกรรมการพิจารณาจริยธรรมการวิจัยใคน					
3.จำนวนคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนที่ได้รับการรับรอง/การยอมรับ					
4.จำนวนคณะกรรมการพิจารณาจริยธรรมการวิจัยในคนที่ได้รับการต่ออายุการรับรอง/การยอมรับ					

ตัวชี้วัด	ความเห็น				
	เห็นด้วยอย่างยิ่ง	เห็นด้วยมาก	เห็นด้วย	เห็นด้วยน้อย	ไม่เห็นด้วย
5.มี SOP การปฏิบัติงาน และเกณฑ์การพิจารณาที่ชัดเจน					
6.จำนวนและร้อยละของคำขอที่พิจารณาอนุญาตภายในเวลาที่กำหนด					
7.ระยะเวลาที่ใช้ในการพิจารณาอนุญาต					
8.จำนวนและร้อยละของคำขออนุญาตที่ยื่นทางระบบ online submission					
9.จำนวนและร้อยละของโครงการวิจัยที่มีเลขที่ Thailand Clinical Trial Registry					
10.จำนวนและร้อยละของคำขอและโครงการแยกตาม phase การวิจัย					
11.จำนวนคำขอและโครงการแยกตามประเภทของยาได้แก่ -ยาที่ยังไม่ได้รับขึ้นทะเบียนที่ประเทศใดมาก่อน -ยาที่ได้รับขึ้นทะเบียนแล้ว แต่มีการเปลี่ยนแปลงข้อบ่งใช้ ขนาด วิธีใช้ยา กลุ่มผู้ใช้ยา -ยาที่ได้รับการขึ้นทะเบียนแล้ว (Phase IV)					
12.ประเมินการดำเนินการตามบทบาท หน้าที่ที่กำหนดจาก -ร้อยละคำขอที่พิจารณาอนุญาต -ร้อยละการตรวจติดตาม -จำนวนการพักใช้หรือเพิกถอนการอนุญาต					
13.จำนวนโครงการที่รับคำปรึกษาจาก อย.					
14.จำนวนโครงการที่รายงานความคืบหน้าภายในเวลาที่กำหนด					
15.จำนวนโครงการที่รายงานการจบโครงการภายในเวลาที่กำหนด					
16.จำนวนโครงการที่มีการบันทึกความคืบหน้าใน Thailand Clinical Registry					
17.สรุปรายงานการเกิด SUSAR ในประเทศไทย					
18.ร้อยละของการรายงานอาการไม่พึงประสงค์ที่ยื่นทางระบบ online submission					
19.จำนวนและร้อยละของโครงการ/สถานที่ถูกตรวจต่อโครงการ/สถานที่ที่เข้า Criteria ในการถูกตรวจประเมิน					
20.จำนวนและร้อยละของการตรวจพบว่าเป็นไปตามมาตรฐาน ICH-GCPและเงื่อนไขการอนุญาต					
21.มีการเพิ่มเติมเนื้อหาเกี่ยวกับ GCP ในหลักสูตร					
22.จำนวน Principle Investigator และ Co-Investigator เพิ่มขึ้นทุกปี					
23.เพิ่มจำนวนศูนย์วิจัยทางคลินิกที่มีคุณภาพ					
24.จำนวนห้องปฏิบัติการที่ได้รับการรับรอง GLP					
25.ความรู้เกี่ยวกับขั้นตอนการพัฒนายาใหม่หรือยาพัฒนาจากสมุนไพร					
26.การเป็นสมาชิก International Clinical Trials Registry Platform (ICTRP) ภายในปี พ.ศ.2557					
27.รายชื่อสถาบันหรือสถานที่ศึกษาวิจัยทางด้าน Non-clinic					
28.มีเว็บไซต์					

ขอขอบพระคุณท่านที่กรุณาสละเวลาตอบแบบสอบถามฉบับนี้ **<u>โปรดกรุณาส่งแบบสอบถามที่โต๊ะลงทะเบียน</u>**

BIOGRAPHY

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