PERFORMANCE INDICATOR DEVELOPMENT FOR PHARMACOVIGILANCE SYSTEM IN THAILAND

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A Dissertation Submitted in Partial Fulfillment of the Requirements
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บทคัดย่อและแฟ้มข้อมูลฉบับเต็มของวิทยานิพนธ์ตั้งแต่ปีการศึกษา 2554 ที่ให้บริการในคลังปัญญาจุฬาฯ (CUIR)
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การพัฒนาตัวชี้วัดผลการปฏิบัติงานสำหรับระบบเฝ้าระวังความปลอดภัยด้านยาในประเทศไทย

นางสาววนิดา แก้วผนึกรังษี

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาเภสัชศาสตร์สังคมและบริหาร ภาควิชาเภสัชศาสตร์สังคมและบริหาร
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วนิดา แก้วผนึกรังษี: การพัฒนาตัวชี้วัดผลการปฏิบัติงานสำหรับระบบเฝ้าระวังความปลอดภัยด้านยาในประเทศไทย (PERFORMANCE INDICATOR DEVELOPMENT FOR PHARMACOVIGILANCE SYSTEM IN THAILAND). อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.ดร.ภูรี อนันตโชติ, 145 หน้า.

การศึกษาวิจัยครั้งนี้มีจุดมุ่งหมายเพื่อพัฒนาตัวชี้วัดผลการปฏิบัติงานสำหรับระบบเฝ้าระวังความปลอดภัยด้านยาในประเทศไทย เพื่อใช้เป็นเครื่องมือในการประเมินผลการปฏิบัติงานดังกล่าวของศูนย์เฝ้าระวังความปลอดภัยด้านผลิตภัณฑ์สุขภาพ การศึกษานี้มีลักษณะเป็นการวิเคราะห์เชิงประเมินโดยออกแบบเป็นการศึกษาภาคตัดขวาง วิธีการวิจัยมี 3 ขั้นตอนหลัก คือ 1) วิเคราะห์ขอบเขตของตัวชี้วัดและนำมาปรับเข้ากับกรอบการวิจัย ซึ่งประยุกต์จากกรอบทฤษฎีการประเมินผลองค์การและกรอบการดำเนินงานเฝ้าระวังความปลอดภัยด้านยา 2) พัฒนาตัวชี้วัดและสร้างเครื่องมือวัดที่แสดงถึงประสิทธิผลและประสิทธิภาพขององค์กร รวมทั้งแสดงถึงปัจจัยทั้งภายในและภายนอกองค์กรที่อาจส่งผลต่อผลการปฏิบัติงานขององค์กร โดยศึกษาจากเอกสารงานวิจัยต่างๆทั้งภายในและภายนอกประเทศ รวมทั้งการสอบถามและสัมภาษณ์เพื่อเก็บรายละเอียดการปฏิบัติงานจากเจ้าหน้าที่ทั้งระดับบริหารและปฏิบัติการ การพัฒนาและปรับปรุงตัวชี้วัดดำเนินไปในลักษณะต่อเนื่องจนกระทั่งไม่มีข้อมูลใดต้องแก้ไขหรือเพิ่มเติมอีก 3) ประเมินความตรงของข้อคำถามและการใช้งานได้ของตัวชี้วัด โดยอาศัยความคิดเห็นจากผู้เชี่ยวชาญในสาขาที่เกี่ยวข้องทั้งภายในและภายนอกองค์กร ที่เข้าร่วมปรึกษาหารือ วิจารณ์ และให้ข้อคิดเห็น อย่างไรก็ตามการคัดเลือกตัวชี้วัดในขั้นตอนสุดท้ายดำเนินการโดยผู้วิจัย

ผลการวิจัยพัฒนาทำให้ได้ตัวชี้วัดและเครื่องมือการประเมิน 4 ด้านคือ 1) ด้านนโยบาย กฎหมาย แผนงาน และโครงสร้างองค์กร ซึ่งแสดงถึงปัจจัยและโครงสร้างหลักที่ส่งผลต่อการปฏิบัติงาน 2) ด้านการเฝ้าระวังความปลอดภัยด้านยา แสดงถึงเครือข่ายการเฝ้าระวังความปลอดภัยและการสืบค้นข้อมูลความปลอดภัยจากแหล่งสำคัญทั้งภายในและภายนอกประเทศ 3) ด้านการค้นหาสัญญาณเตือนภัยเพื่อใช้เป็นข้อมูลประกอบการตัดสินใจกำหนดมาตรการบริหารความเสี่ยง และ 4) ด้านการสื่อสารข้อมูลความปลอดภัยแก่ผู้เกี่ยวข้องเพื่อให้เกิดความตระหนักและใส่ใจต่อการใช้ยาอย่างถูกต้องและเหมาะสม

ตัวชี้วัดดังกล่าวยังอาจแบ่งออกได้เป็น 3 ด้านคือ ตัวชี้วัดด้านโครงสร้าง 10 ตัว ตัวชี้วัดด้านกระบวนการ 5 ตัว และตัวชี้วัดด้านผลลัพธ์ 6 ตัว แม้ตัวชี้วัดส่วนใหญ่จะให้ผลในเชิงปริมาณ แต่ในการแปลความหมายก็มีความจำเป็นจะต้องอาศัยข้อคำถามเชิงคุณภาพมาประกอบเพื่อให้เกิดความเข้าใจที่ชัดเจนยิ่งขึ้น อาจกล่าวโดยสรุปได้ว่าเครื่องมือการประเมินที่พัฒนาขึ้นนี้สมควรที่ผู้เกี่ยวข้องในระดับต่างๆจะได้นำไปทดลองใช้และปรับปรุง เพื่อใช้เป็นหลักในการประเมินผลองค์กรต่อไป

ภาควิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่อนิสิต .....

สาขาวิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่ออ.ที่ปรึกษาวิทยานิพนธ์หลัก.....

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4977102033: MAJOR SOCIAL AND ADMINISTRATIVE PHARMACY
KEYWORDS: ORGANIZATIONAL PERFORMANCE ASSESSMENT / PERFORMANCE INDICATOR / PHARMACOVIGILANCE

WANIDA KAEWPANUKRUNGSI: PERFORMANCE INDICATOR DEVELOPMENT FOR PHARMACOVIGILANCE SYSTEM IN THAILAND. ADVISOR: ASST.PROF. PUREE ANANTACHOTI, Ph.D., 145 pp.

The goal of this study was to develop a set of indicators to assess the performance of the national center for pharmacovigilance in Thailand. The study was initiated to respond to the need of systematic evaluation of phamacovigilance system, but the lack of comprehensive tools. The indicators were designed based on the theory of organizational performance assessment and pharmacovigilance functioning framework. This is an evaluative analysis study based on cross sectional research design. The indicators were developed based on three-stage model: 1) applying logic model and identifying indicator domains, 2) formulating the candidate indicators, and 3) validating the selected indicators through expert opinions.

21 indicators were developed and judged against two validation criteria: relevance and practicability. The set of validated indicators consisted of four domains:

1) **policy, law, plan, and structural support**, this domain comprised 9 indicators, which could be used to identify the existence of and the relevance of legal provisions, policy, and plans, and to examine the organizational structure. They reflected the enabling factors to enhance the successful towards the organizational goals.

2) **safety surveillance**, comprised 5 indicators. The indicators reflected the capability of the organization to participate and build partnerships, and bring multiple stakeholders together for successful information exchange. They referred to the coordination and collation of data between data providers and the national center, timely and effective data flow, as well as the quality of data obtained from secondary sources.

3) **signal detection and decision making for risk management**, comprised 4 indicators: data preparation to be analyzed, data quality, automated signal detection and decision making for risk management. This domain referred to the function of the NPVC to collect, summarize, and transform of ADR information; to identify, estimate, and evaluate the volume and seriousness of risks that associated with a pharmaceutical product; and to propose the corrective measures to minimize risks. They reflected the capability of the organization to manage large dataset and make decisions for risk management.

4) **communication of safety information**, comprised 3 indicators. The indicators reflected the capability of the organization to organize timely and effective dissemination of safety information, and its responsiveness to any related queries either in domestic or international level so as to facilitate safety surveillance.

The developed indicators could be divided into 3 types: 10 structure indicators, 5 process indicators, and 6 outcome indicators. Most of the indicators were yes/no questions or percentage/rate measurements, subsequent qualitative data from the respondents were needed for better interpretation of the results. It could be concluded that the developed assessment tool should be tested and refined in order to be routinely used for the organizational performance assessment in the future.

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Student's Signature.....
Advisor's Signature.....

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LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
AEFI	Adverse Events Following Immunization
BKK	The Bangkok Metropolitan, Thailand
CIOMS	Council for International Organizations of Medical Sciences
EMEA	European Medicines Agency
HPVC	Health Product Vigilance Center (Thailand)
ICH	International Conference on Harmonization of Technical Requirements
ICSR	Individual Case Safety Report
INECE	International Network for Environmental Compliance and Enforcement
ISoP	International Society of Pharmacovigilance
MAH	Marketing Authorization Holder
MedDRA	Medical Dictionary for Regulatory Affairs
MoPH	Ministry of Public Health
NDA	National Drug Authority
NDP	National Drug Policy
NHSO	National Health Security Organization
NPVC	National Pharmacovigilance Center
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
SMP	Safety Monitoring Program in Thailand (for new chemical entities)
SOP	Standard Operating Procedure
SUSARs	Suspected Unexpected/Unlabeled Serious Adverse Reactions
ThaiFDA	Thai Food and Drug Administration
UMC	Uppsala Monitoring Center, WHO Collaborating Center for International Drug Monitoring
USAID	The United State Agency for International Development
USFDA	The United State Food and Drug Administration
WHO	World Health Organization
WHO-ART	WHO-Adverse Reaction Terminology

CHAPTER I

INTRODUCTION

1.1 Background and Rationale

The pharmaceutical sector is a high-technology and knowledge-intensive industry. The sector produces and distributes chemicals with therapeutic value. Pharmaceutical products are an important input into healthcare services. Since the objective of public health regulation is to diminish a significant risk to human health, the pharmaceutical industry is heavily regulated. The regulatory measures are major tools or strategies using to guarantee the safety of medicines.

At the national level in Thailand, the Thai Food and Drug Administration (ThaiFDA) plays a vital role in pharmaceutical control. The mission of the ThaiFDA is to regulate and ensure that the available medicines are safe and effective. The mission is accomplished from the early stages of drug review and approval to surveillance of the product when it launches in the market. While the ThaiFDA is a scientific-based agency, it is also a law enforcement agency. The ThaiFDA is in charged with enforcing the Drug Act, its regulations, and some related health laws. The agency is responsible for assessing the safety, efficacy, and quality of the pharmaceutical products in pre- and post-licensed phases. It is also responsible for proposing to the Minister of Public Health and enforcing the legal measures to manage risks from drug use, such as product reclassification and restriction of drug distribution, regarding the severity of known or unknown adverse effects. The ThaiFDA also has the authorities in approving and monitoring labels, package inserts and advertisement of medicinal products, so that the practitioners and consumers are provided with accurate and adequate warnings and precautions for safe use. Moreover, the agency has responsibility to oversee drug selling by personnel in charge at community drug stores in some aspects, which accounted in a small part of good practices in pharmaceutical dispensing.

Drug risks can be generated by different sources, including product quality defects, medication errors, and adverse drug reactions (ADRs). Obligatory responsibilities are imposed on drug industry, regulatory authorities, and health practitioners to ensure that the medicines are safe when used as intended. In some countries, safety monitoring and risk management interventions to prevent drug risks are implemented by means of legislation, such as pharmaceutical laws, consumer protection, and professional practice. Prevention of drug risks involves a wide range of activities. Although risk minimization strategies may be different among countries, the general processes to reduce risks are quite similar. Initially, the measures aimed to promote safe use of medicinal products encompass pre-clinical and clinical studies in the development of new drugs, then post-licensed surveillance, risk assessment, and re-evaluation by national authority are conducted, as well as control of drug distribution, promotion and advertising. In addition, quality assurance activities, including control of prescribing, dispensing, and pharmaceutical care via professional practices are carried out in hospital settings and community drug stores.

The ThaiFDA's activities are prioritized based on benefit- risk to public health. Products with a severe health hazard to the user are its highest priority. Such products include those indicating a potential for causing serious adverse effects, or those displaying the evidence of injury or fatal outcome. The main activity under the ThaiFDA's mission is post-marketing surveillance for drug safety. Pharmacovigilance (PV) program has been established at the national level in Thailand since 1984. The role of the national ADR monitoring center is to gather reports and other sorts of information concerning ADRs from domestic and international sources. All of these information are subsequently analyzed, interpreted, and used to guide decisions on proper risk management measures at the national level.

Pharmacovigilance systems have been established at supranational and national level in developed and developing countries to monitor, analyze, assess and prevent adverse effects or any other drug-related problems (WHO, 2002). Structures and processes of the systems vary from country to country. Generally, health personnel are expected to observe the outcomes of drug use and report the adverse

effects, if they occurred. In some countries, reporting is mandatory, while most countries adopted voluntary reporting approach. Some countries emphasize more on the surveillance of rare and serious adverse effects, or newly marketed medicines. Most of the surveillance systems worldwide are spontaneous voluntary reporting by health professionals, thus ADR is under-reporting and true incidence of undesirable effects caused by pharmaceutical products is unknown.

At the international level, following the thalidomide disaster of the late 1950s, when there were few national and no international systems for monitoring adverse drug reactions, the World Health Assembly set up the WHO Program for International Drug Monitoring. The intention was to prevent any such adverse event to happen again by ensuring that any safety signal would be rapidly recognized through a central clearing-house and acted by individual countries.

Starting with a group of ten countries, the WHO Program now includes more than a hundred member countries and a further twenty as associate members. The Uppsala Monitoring Centre (UMC) is responsible for the program in Uppsala, Sweden. At the Centre (UMC), the WHO International Database (VigiBase) is held and regularly updated with ADR reports from member countries. It is screened for any pattern of suspected problems across the world and member countries are notified when there are issues which need attention. VigiBase holds more than five million ADR reports from all over the world. The UMC also arranges the annual meeting of member countries and a range of other technical, communications and development services.

Thailand became the 26th member of the WHO Programme in 1984. The Adverse Drug Reaction Monitoring Centre (ADRMC) was set up and managed by the Food and Drug Administration (FDA). The name of the Centre was changed to the Adverse Product Reaction Monitoring Centre in 1997, in recognition of widened responsibilities, and, most recently, to the Health Product Vigilance Centre (2008).

At present, the pharmacovigilance system in Thailand is managed by the Health Product Vigilance Centre (HPVC) as the National Pharmacovigilance Center (NPVC) of the country. It is under the Technical and Planning Division of the Food and Drug Administration (ThaiFDA) in the Ministry of Public Health (MoPH). The overall purpose of the Health Product Vigilance Centre (HPVC) is the reduction of risk to patients and consumers and the improvement of the safety and effectiveness of health products.

Products within the responsibilities of the HPVC include: medicinal products, herbal and traditional medicines, narcotic and psychotropic substances, foods, cosmetics, medical devices and hazardous substances used in household and public health. The HPVC is also a focal point of Adverse Events Following Immunization (AEFI), parallel to the Department of Disease Control, Ministry of Public Health (MoPH). In most countries, surveillance centers carry out only pharmacovigilance (widely known as adverse drug reaction monitoring), however in Thailand, the Centre has wider responsibilities, extending to cover all health products. The Centre has coordinating responsibilities for all health products but has particularly focused on medicines.

The HPVC is responsible for the safety surveillance of health products particularly medicines, including herbal and traditional medicines, through the collection of adverse drug reaction (ADR) reports and conducting of research. Product surveillance is carried out using several methodologies, including spontaneous reporting, intensive monitoring, pharmacoepidemiological research, and registry for specific groups. Adverse reaction reports are collected nationwide directly from health facilities or channeled through a national network of regional centers located in 18 tertiary hospitals in rural areas. The regional centers are responsible for determining causality of drug-ADR pairs, while the HPVC manages signal detection for suspected drug-ADR associations. The HPVC provides the Thai Food and Drug Administration (ThaiFDA) with information about problems with health products in order for the national authority to take appropriate risk management actions by withdrawing products, adding warnings, amending labeling or packaging, restricting

prescribing criteria or use, and other methods. Safety issues are disseminated throughout the country on a routine basis, and as urgent news when necessary.

In general, some ADRs are known, while some are unexpected when the drug gets approval. It is not possible for a particular drug to be well tested and completely reviewed for its safety so that it can be used without risk-taking. Thus, safety does not mean zero risk (USFDA, 2003). There have been a lot of drugs withdrawn from the global market due to safety reasons, even after launching for only a few years. For example, rofecoxib (Vioxx®) was withdrawn from many countries because of the increased incidence of myocardial infarction.

The PV system in Thailand collects reports of suspected problems and actively researches issues of concern. When problems are identified by the HPVC, the Drug Committee (or appropriate body) uses this information to make recommendations for subsequent decision and action by the FDA. Such action includes withdrawing products from the market, enforcing labeling, prescribing or other changes, inspection of manufacturing facilities, and other methods. Communication of new information to healthcare professionals about the benefit and harm of products is an essential element of the work. Over the past several years, many regulatory actions due to various safety issues have emerged from PV activities in Thailand, both benefited from domestic and international information (the HPVC booklet (draft), 2011) such as:

- Withdrawal/prohibition of manufacturing or distribution:
    - Single active formulation of Keelek (*Cassia siamea* L.) due to hepatic injury
- Reclassification/restriction of use:
    - Cisapride – drug interaction causing potential risk of QTc prolongation
        - from prescription to controlled drug (hospital use only) and restricted indications only for treatment of gastroesophageal reflux disease
    - Parecoxib - serious adverse event, fatal outcome (often in elderly)

        - restricted post-operative use and continuous use for maximum of 3 days
    - Aspirin - Rye's syndrome & GI bleeding (in children)
        - restricted use for adults only
        - leveraged drug class to special-controlled drug (prescription drug only) except for use as analgesic and antipyretic
- Label and package insert changes and warnings:
    - Propylthiouracil-induced agranulocytosis
    - Ethambutol – visual disturbance
    - Bupivacaine (spinal block) - serious AE, fatal outcome
    - Antituberculosis drug – serious AE, hepatitis
- Risk communication
    - Safety alert : Neo-optal eye drop (antibiotic with corticorsteroid) - Superficial Punctate Keratitis
    - Alert to monitor of drug usage: resperidone - attempted suicides, deep vein thrombosis

Almost 30 years, pharmacovigilance system in Thailand has been developed in many aspects. The volume of ADR individual case reports have been increasing, from around 280 reports in 1984 to 38,698 reports in 2008, accumulating more than 270,000 records and approximately 35,000 reports per year, accounting to the nineteenth of top twenties ranking in Vigibase of the World Health Organization (WHO) collaborating Center for International Drug Monitoring Program (UMC Report, 2009). However, the quality of information generated from such reports, the organizational performance, the outcomes and impacts of the program are still questioned. Evidences from voluntary reports and intensive studies revealed the occurrences of under-reporting and the ineffectiveness on the enforcement of the regulations to minimize drug risk. Studies in many hospitals demonstrated that a large number of Thai people were admitted to the hospitals or extended the hospitalizations as the results of drug-induced injuries, including ADRs. The research findings also showed that many of those drug-induced problems were expected and preventable (the HPVC booklet (draft), 2011).

Over the past few years, the criticism was raised by the media about the failure of pharmacovigilance systems on risk prevention (Edwards and Isah, 2011). Many countries on both sides of the Atlantic have called for more effective PV to manage risk and PV information in the proactive ways, as well as to develop effective analysis tools. The case of rofecoxib (Vioxx®), previously mentioned, was an example of ineffective PV. Because the drug was very widely used and heart attack may cause fatal outcome, the impact of this problem was a big issue in public health concern. However, many DRAs had been taking action too slow. An early warning could be seen earlier in the product literature. The slow action was from a complex decision making and ineffective communication (Edwards and Isah, 2011).

For those reasons, performance assessment of the NPVC is needed since it takes the central role for PV development in the country. The assessment will identify the effectiveness and efficiency of the organization, provide motivation and direction, give feedback of its execution, and help in strategy formulation and revision. Such the evaluation will provide the answers whether the organization is implementing consistently with the way it was envisioned, and how well it is functioning, if not, what are the particular issues that either facilitate or inhibit the organizational ability to effectively put the PV program in place to mitigate drug safety problems.

According to the lack of comprehensive set of indicators to use in assessing the performance of the NPVC, performance indicators are needed to be designed and developed. The indicators can be used by managers of the NPVC to support a performance assessment for monitoring its operations in order to adjust its strategies and to allocate appropriate resources. The NPVC itself can use the indicators to enhance accountability to stakeholders and the public. Policymakers and leaders can use the indicators as a management tool to lead and direct the organization. Government budget authority can use the indicators to make decisions about resource allocation. Stakeholders can use the indicators to enhance the NPVC to carry out its mission.

This study aimed to develop the set of comprehensive indicators in order to use as a future assessment tool to evaluate and assess the performance of the national centre for pharmacovigilance, as well as to help monitoring PV implementing in Thailand. Organizational assessment model was employed as the conceptual framework for indicator development and three-stage model as the stepwise method to develop and validate the combination of the candidate indicators.

1.2 Objective

The study aimed to develop the set of performance indicators to measure the effectiveness and efficiency of the NPVC in Thailand, and to be used as a future assessment tool to monitor and assess the organizational performance.

1.3 Scope of the study

1) The study is focused on the organizational level and scoped at the national center for pharmacovigilance (NPVC), responsible for post-licensing pharmacovigilance program in Thailand.
2) Drug-related problems are scoped only in adverse drug reactions (ADRs), thus medication errors, product defect, overuse, misuse, or others are excluded.
3) Drug safety surveillance in clinical trials and other specific pharmacovigilance programs are excluded.

1.4 Expected benefits and significance of the study

1) Performance indicators will be invaluable to use as an instrument to help managers of the NPVC assess the organizational work, and determine what needs to be carried out to achieve its desired goals.
2) Performance indicators can help monitoring organizational operations in order to ensure the appropriate uses of its resources to accomplish the organizational goals.

3) Performance indicators can be used to motivate staff of the NPVC to accomplish the organizational goals.
4) Results from the utilization of performance indicators can enhance the accountability of the organization to various stakeholders and the general public.

CHAPTER II

LITERATURE REVIEW

The literature reviews of this study were performed to assist the development of the set of performance indicators to help assessment and evaluation the overall performance of the national pharmacovigilance centre in Thailand. The contents of this chapter aimed to identify concept and definitions of the important terms used in pharmacovigilance area, including the principles of risk management, and good practice in pharmacovigilance activities. The general models for organizational assessment and evaluation, organizational performance assessment, and the methods and procedures for developing and validating indicators will be briefly described. The structure of this chapter comprises these components:

1) The systems of pharmacovigilance
2) General models for organizational assessment and evaluation
3) Organizational performance assessment
4) Three-Stage model for development of performance indicators

2.1 The systems of pharmacovigilance

The World Health Organization defined pharmacovigilance as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problems (WHO, 2002)”. “Pharmaco” came from the word “pharmacology” that is the study of the effects of drugs, so it obviously means “drug-related”. “Vigilance” is derived from the Latin word “vigilare” which means “to be alert” or “to pay attention”. In the pre-licensing phase, the pharmaceutical products are tested by a limited population, but the marketed medicines are widely used by a more diverse population. The aim of the pharmacovigilance activities is to improve safety of the marketed medicines by collecting all information about drug risk, especially rare adverse reactions, to generate safety signal as soon as possible.

The international pharmacovigilance program has emerged since the 1960s after the thalidomide disaster. The main activities of the program are to systematically collect and analyze adverse events linked to drug uses via spontaneous ADR reporting or other pharmacoepidemiological studies. The processes aim to provide evidence to identify signals, analyze the emerging problems, using the evidence to make decision on risk minimization and prevention, and finally communicate the safety alerts or warnings to the general public. These processes involve many kinds of stakeholders, especially patients, healthcare professionals, drug regulatory authority, and pharmaceutical industry.

At the international level, the WHO program for international drug monitoring at the Uppsala Monitoring Center (UMC) collates adverse drug reaction reports, submitted through the Vigibase online system by the national pharmacovigilance centers (NPVC) of the member countries. Although a lot of medicines have been heavily consumed in the developing countries, drug safety profiles that have been distributed from developed countries could not be generalized due to the remarkable differences in the local contextual and genetic influences. Thus, it is vital to establish the pharmacovigilance system in every country, especially in the developing world, in order to identify health hazards as soon as possible.

The principles of pharmacovigilance have been employed and implemented in the foundation of risk management activities. Although marketed pharmaceutical products are expected to be safe, it is impossible that they have no risk at all. A safe product means the one that has acceptable risks, comparing to the expected benefit. Thus a safe medicine tries to balance its risk-benefit in the healthcare system.

Under the current system worldwide, pharmaceutical products must be approved before marketing by the national regulatory agency. The pre-marketing review processes require that the drug is safe and effective by evaluating data that the marketing authoritative holders (MAHs) submitted to determine whether the product achieves the standard criteria for legal approval to launch in the market. Another aspect of the pre-marketing evaluative processes is the approval of product labeling.

The labeling must indicate who are suitable for treatment, identify the potential risks especially serious ADRs that might cause fatal outcome, and explain the way the product should be used.

After approval processes, products could launch into the market and ready to be used by prescribers and patients. “While the regulatory agency evaluates the risks and benefits for the population, the prescriber takes the major role to manage risks and benefits for the individual” (USFDA, 2003). In the situation of a decision making for patient treatment, the regulatory agency takes the indirect role in reducing risks by ensure that the prescriber and the patient have enough risk-benefit balanced information about an available pharmaceutical product.

The general objective of post-marketing surveillance programs are to identify unexpected risks related to the approved products. If the detected risks are more serious than the acceptable level, there may be a re-evaluation to make decision again about drug approval.

2.1.1 Concept of risk

The International Conference on the Harmonization of technical requirements for quality risk management, and adopted an ISO definition of risk as the combination assessed, and controlled in the context of pharmaceutical quality. However, WHO defines risk as the probability of developing an outcome that normally, but not always occurred. Contrary to “risk”, harm is the damage qualified by measurements of frequency of occurrence, severity or duration (Lindquist, 2007).

Formal definitions of risk, which can be demonstrated by the Probability × Severity concept, focus on the conditional probability of harm, given that exposure to a hazard occurs (Claycamp, 2007). Hazard refers to the property of a substance or event to cause harm, suggesting that hazard exists independently of risk. In ICH “Quality Risk Management”, hazard was defined as the potential source of harm. The link between hazard and risk is as the example: finding microbial contamination on

external surfaces of sterile filtration apparatus is the evidence of hazard but not of direct risk to the patient. This statement includes the possibility that historical data might show that external contamination is associated with an increased likelihood of internal contamination of sterile contents, that are the potential for a more direct risk pathway. Finding contamination within the sterile drug, as the exposure pathway, is direct evidence for increased risk to the patient.

In general, it is difficult to measure risk directly in exposed population, although the goal in risk management is to link risk to the patient. This leads to find out simpler surrogate measures. Programs such as Good Manufacturing Practices (GMPs) are established on an assumption that managing drug quality, using of surrogate measures, such as quality parameters in the production process, can help to manage risk to the patients from drug quality defects. By using a broad definition of risk – a combination of the probability of occurrence of harm and the severity of that harm– implies that risk-risk comparisons can be depicted as the following (Figure 2.1, from Claycamp, 2007):

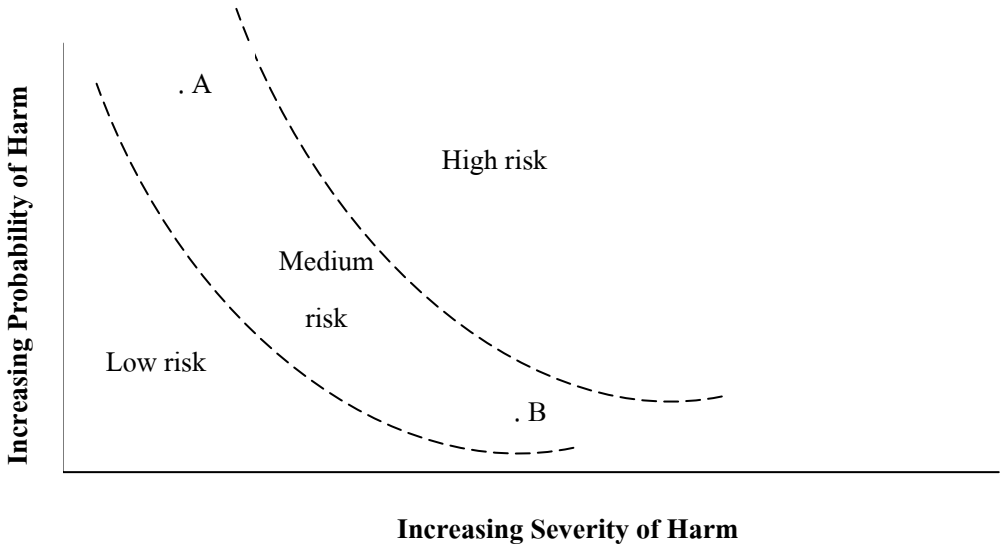

Figure 2.1: the level of risk from the probability and severity of damaging events

From figure 2.1, bounded regions of low, medium, and high risk are shown. The property of mathematical reciprocity is between probability and severity of the event in determining risk: point A is for a risk that is of high probability but low severity. The same level of medium risk for point B is shown with a high-severity but low-probability risk. Risk-risk comparisons could encourage the government, pharmaceutical industry, and the general public to search for the severity weightings (values) for different types of risk and harm. For example, risk could range the severity from a failure to relieve dermatitis using a medicated skin cream to fatal outcome from an injectable drug. It is debated on a society level how many cases of skin rash is risk-equivalent to one case of death from a life-saving medicine.

2.1.2 The principles for risk management

The systems of pharmacovigilance can be explained by risk management concept. In general, risk management is a systematic concept dealing with policies, procedures, and practices in identifying, assessing, analyzing, treating, monitoring and communicating risk to life, property, or other valuables. Objective information from analytical tools, including risk assessment, benefit-cost analysis, trade-off analysis, or quantitative decision analysis, along with the subjective values of stakeholders, are employed to make decisions on controlling, eliminating, or accepting risk. In practice, quantitative risk analyses are only part of the information used by decision makers in choosing risk minimization strategies from a set of decision options based on broad social, economic and political issues.

The principle components of risk management are risk assessment, risk control, risk review, and risk communication. A more practical level was drawn in the following process flowchart (Figure 2.2).

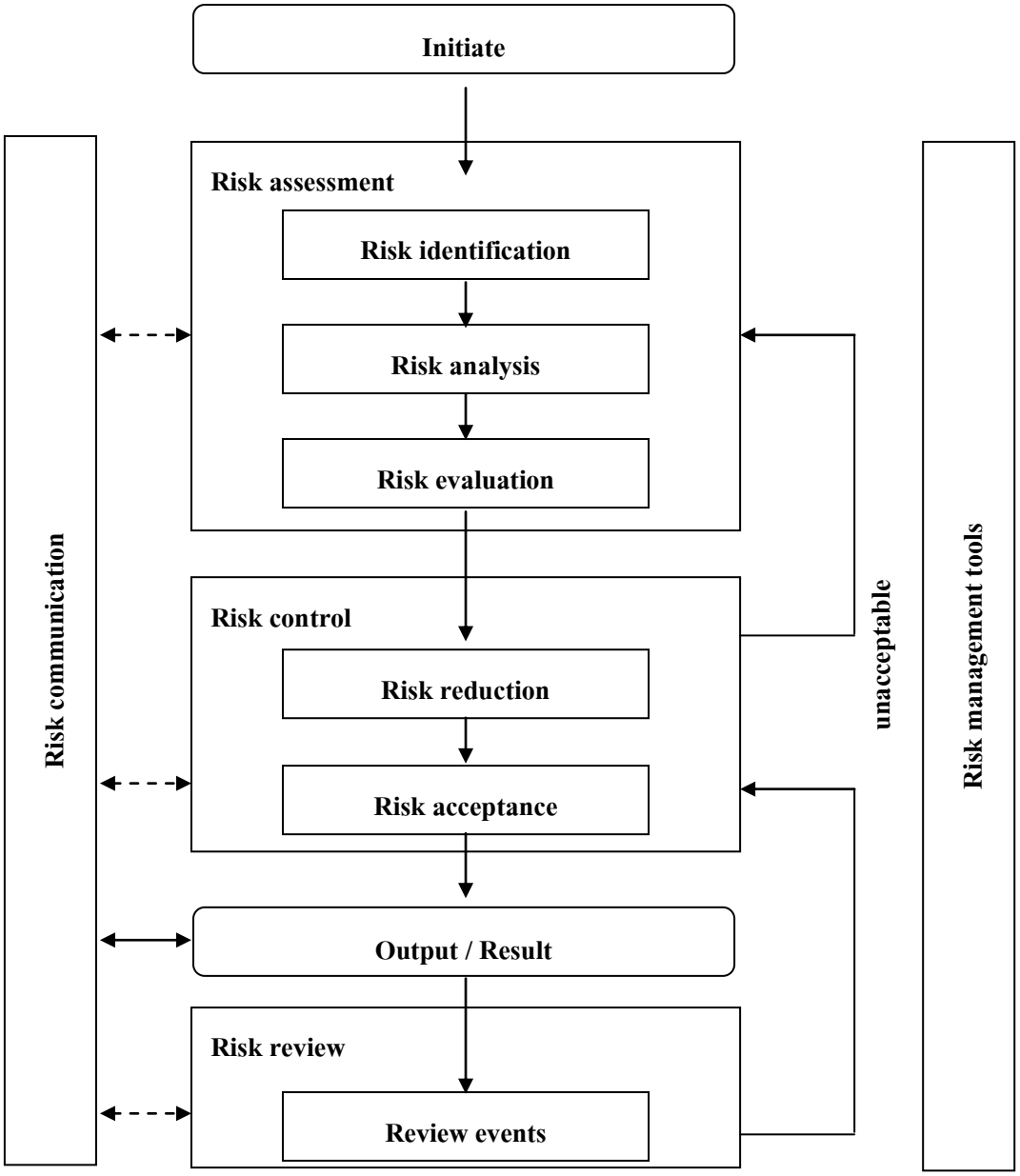

Figure 2.2: risk management process flowchart (USFDA, 2003)

From figure 2.2, when the risks of interest are defined or the problems are scoped, the relatively analytical steps of risk identification, risk analysis, and risk evaluation are undertaken. Risk control includes decision steps to implement risk reduction or to find that a risk is acceptable, such as below a currently acceptable level. The unacceptable arrow in the flowchart shows that an iteration of risk

assessment is undertaken to collect all information and to determine whether the risk controlling strategies could reduce risks as intended. A significant difference between risk management and risk assessment is that risk management includes decisions to either mitigate risk, accept existing risk, or even to do nothing (maintain status quo). Thus, risk management theory shares many concepts and principles with decision analysis and sometimes is referred to as decision making under uncertainty.

Risk review indicated that risk management is an ongoing and iterative process. Effective risk communication can provide and share better information and enhance more informed decisions among decision makers and other stakeholders. Communication is widely viewed as essential from internal communication among teams and in executing risk management programs. “Report” is some kinds of the output of risk management that is communicated. Reporting may not only be as a function of severity and probability of the risk, but also as a function of analytical complexity of risk management processes. The form and content of the communication depends on the audience and the audience’s needs.

The model for pharmacovigilance system can be explained by the risk management processes. These include risk identification and assessment, risk reducing strategies or interventions, risk communication, and monitoring and evaluating the results of the interventions and communications. The details of activities are described as the followings:

Risk Assessment*: risk estimation and analysis*

In pre-marketing phase, risk assessment aims to identify and quantify risks related to a medicine before the product launching in the market. This occurs during clinical development. The known risks are then determined in the approval decision and illustrated in the labeling and package insert of the approved product. In the post-marketing phase, risk assessment is also the program for assessing risks, but focused on new and unexpected adverse reactions that were not be detected before marketing

The program relies basically on the programs of adverse reaction monitoring system in the country.

Risk Confrontation*: identifying acceptable level of risk among affected communities*

Affected communities may perceive drug risks and benefits differently from the regulators. AIDS patient groups and cancer groups may judge the volume of tolerable uncertainty differently from other groups. Patients with life-threatening illnesses may accept a high degree of risks against the benefits of new medicines, while other advocacy groups, such as child-school vaccination, may perceive that even a few risk is unacceptable. Thus, social and community perception are as important as the expert's technical judgments and should be included to determine the level of acceptable risk.

Risk control Intervention*: risk reducing strategies*

Risk reducing interventions are alternative control actions, selected to minimize or manage risks. During the pre-marketing period, regulatory authority is responsible for the marketing approval decision. If the risk of a product is determined to be more than its benefits, the agency can prevent people from those risks by not allowing it to entry the market. After marketing, if new information changes the risk-benefit balance, the regulatory agency can take any risk reducing actions, such as drug withdrawal, or suspension of its license. Control actions include the regulation of product labeling, advertising, promotion, and also additional restrictions on drug use.

Risk Communication*: interactive processes of exchanging risk information*

This is a sharing process of exchanging safety information. Effective communication helps affected advocacy groups make more informed decisions. The important communication tool has been the approved package insert and labeling, targeted to the physicians and other healthcare professionals. However, direct-way

communication with consumers and patients should be considerably initiated, as well as increasing the activities that enhance a two-way communication of safety information among healthcare communities.

Risk management Evaluation*: evaluate effectiveness of risk management strategies*

Any system demands performance measurement including an evaluation phase in order to monitor and assess its effectiveness. The results from the evaluation processes can be used to determine whether the system is well performing or not. The assessment indicator to measure performance includes monitoring changes in drug prescribed related to the rate of adverse events from drug uses.

2.1.3 Good practice in pharmacovigilance

Good pharmacovigilance practice is the general guideline for the NPVC to manage PV activities. It could be viewed as a standard guidance for any NPVC to follow in order to improve work processes and its entire performance. Complete data from spontaneous ADR reporting system is the starting point for good PV practice. Many reports are developed to be case series, and then may generate new signals. However, a single complete case report can generate a signal. Signals refer to the increasing volume of the associated drug-ADR pairs that would significantly occur higher than the expected. Well-documented case reports of ADR and data from other sources, such as the medical literature, clinical studies, or the DRA (Drug Regulatory Authority) in other countries could be used to generate signals of adverse effects related to medicines. Thus, the completeness and quality of the ADR report is the critical part of PV practice.

Good reporting practice

It is important for trained healthcare practitioners, as the reporters, to submit complete information of ADR case reports either in the initial detected events or the

subsequent follow-up, especially for SUSAR events. The good characteristics of a case report should comprise the following elements (USFDA, 2003):

1. The specified adverse drug reactions, including time to onset of the symptoms
2. The details of suspected and concomitant drug therapy (including dose, lot number, date and duration of drug uses)
3. Patient characteristics, including demographic information (e.g., age, gender, race), baseline drug therapy, co-morbid conditions, family history relating to the disease, and other risk factors
4. Clinical outcome of the events (e.g., hospitalization or death)
5. Laboratory data relating to the drug therapy
6. Dechallenge or rechallenge of drug therapy
7. The diagnosis methods of the events;
8. Any other relevant information (e.g., other details relating to the events)

Developing and descriptive analysis of a case series

Initially, a review of the cases is suggested to be carried out. Then search for additional cases, if needed, should be performed through the published literature, and other available databases such as Vigibase. After that, standardized case definitions, such as inclusion or exclusion criteria for a case, could be used to assess potential cases to include in a case series. Other investigations or analyses on the clinical content and completeness of the ICSRs, as well as the examination of a causal relationship between drug and ADR should be carried out. Additionally, in the event that more additional investigations are needed, a case series should be employed to identify potential risk factors. A case series should include an analysis of the following elements (USFDA, 2003):

1. Clinical and laboratory data relating to the events
2. Demographic data indicating the characteristics of patients with the events (e.g., age, gender, race)
3. Drug exposure duration

4. Time to onset of the events due to drug exposure
5. Doses of drug therapy
6. The route of drug administration (e.g., oral, injection)
7. Lot numbers, if available, for products used in patients with the events
8. Use of concomitant medications
9. The underlying co-morbid conditions, such as hepatic or renal impairment
10. Other related information such as ADR reporting rate that changes over calendar time

Signal detection, risk identification and assessment

At the stage of signal detection, risk identification, and risk assessment, the methods of data mining can be used to help generating safety signal. Data mining is the systematic examination of the association of drug-ADR pairs by applying statistical or mathematical tools. Applied data mining techniques could be used to identify unusual or unexpected drug-ADR combinations that needed further investigation. Data mining is also useful for identifying patterns and time trends of the events.

The methods of data mining usually generate a score that quantifies the disproportionality between the observed and expected values for a given drug-ADR combination. Various data mining approaches may be used, such as the Multi-Item Gamma Poisson Shrinker (MGPS) algorithm, the Proportional Reporting Ratio (PRR) method, the Reporting Odds Ratio (ROR) method and the Neural Network approach. However, voluntary adverse reaction reporting systems may be influenced by a variety of reporting biases, the results from any of these approaches should be interpreted with caution. Safety signal should be careful considered with these particular occurrences: unlabeled or previously unrecognized adverse reactions, serious or rare events.

After identifying a safety signal, a careful review and summary of the case series should be performed descriptively. A synthesis of all available safety

information, including clinical findings and current observations, would be presented and interpreted. In order to help interpretation, the case reports should be presented with denominator or exposure information, background rate, relative risks, odds ratios, or other measures of association, and marketing experience with products in the similar class, etc.

Risk assessment is the process of identifying, estimating, and evaluating the probability and severity of risks associated with a pharmaceutical product. The assessment would be considered regarding the available relevant information from various sources. The assessment of benefit-risk balance should involve these particular factors: strength of the association, temporal relationship between drug use and the event, biological plausibility, feasibility of further studies, or benefit that the medicine can provide, including other alternative therapies.

Decision making for risk minimization tools

According to the limitation of the general population using medicines before approval and unexpected risks that may happen after a product is launched in the market, ADR reporting systems become the important sources of safety information. Risk minimization strategies are designed to enhance prevention drug risk in at-risk population, as well as encouraging reasonable drug utilization in the society. Making decisions about risk reducing tools are based on scientific and logical factors, including the frequency of the event occurs (e.g., incidence rate, reporting rate, or other measures available), the severity of the event, the nature of the population at risk, the method by which the medicine is dispensed (through pharmacies or via restricted distribution channels only).

Risk communication and risk minimization tools

In order to ensure the safe use of marketed medicines, effective strategies to minimize known drug risks are required. Most of the regulatory agencies around the world developed various strategies to reduce and /or eliminate drug risks. It can be

noted that there are 2 main types of the strategies; risk communication tools and regulatory action tools.

For communication tools, the regulatory agencies would encourage drug manufacturers to develop relevant labeling and drug information materials, such as drug leaflet, package insert or the cover of the box. Information required for safe use of certain drugs includes serious adverse events or the directions to guide patient adherence that are deemed crucial to the effectiveness and /or safe use of the medicine. Risk communication tools used in the past and present are (1) patient package inserts (PPIs), which are part of FDA-approved labeling in order to provide drug information; (2) patient information leaflets (PILs), known as consumer medication information leaflets, which are preprinted or often non-FDA-approved drug information materials written by a vender other than drug manufacturers and dispensed to patients for educational purposes; and (3) “Dear Healthcare Professional (DHCP) letters”, which are distributed to relevant parties to convey new safety information. Other tools include “Press releases”, “Drug bulletin”, or education for prescribers and healthcare practitioners on annual pharmacovigilance symposium, etc.

Other efforts beyond these established risk communication tools often require changes in some prescribing practices by physicians and in the dispensing of prescriptions by pharmacists. Risk minimization strategies generally include traditional risk communication along with additional efforts on regulatory actions. The regulatory actions developed for minimizing risk include restricted distribution of products (e.g. prescription only by specialists in hospitals), asking pharmaceutical licensing holders to conduct post-marketing observational studies, suspension of drug delivery, change drug categorization (e.g. from OTC to prescription), marketing intervention (e.g. pack size restriction), drug licensure withdrawal or suspension, etc.

It could be summarized that good pharmacovigilance practice could be clearly and well explained by risk management process. Risk management is an ongoing, stepwise and iterative process. Steps, occurring in logical sequence, may start with the investigation of a potential risk, the assessment of benefit-risk balance of the drug,

and the implementation of risk minimization actions. Risk communication and the assessment of strategies to minimize product risk should also be carried out.

2.1.4 Pharmacovigilance program in Thailand

Most of the pharmaceutical safety information needed for signal generation and risk assessment was generally transferred from data collection system in western countries. According to socio-biological variations among Thais and western people, such as genetics, consumption behavior and other epidemiological factors, the pattern and severity of adverse drug reactions occurring in Thailand and in western countries were not similar. For these reasons, the establishment of Thai national pharmacovigilance program to collect and analyze drug safety data in Thais was rational.

The general purpose of pharmacovigilance program are to encourage risk identification and assessment, promote safe use of medicines and effective communication of safety information through education and training in pharmacovigilance in order to improve public health and patient care (WHO, 2002).

In 1980, Thailand initiated a pilot project for adverse drug reaction monitoring in some hospitals under the Ministry of Public Health and two medical schools. In the year 1983, the Ministry of Public Health officially set up the Adverse Drug Reaction Monitoring Center under the responsibility of the Food and Drug Administration. Monitoring system was also set up in order to detect adverse drug events and could be operated since 1984. The ADRM center collected and analyzed the information on the risks and adverse reactions related to medicines, employing the theory and applications of epidemiology and appropriate statistics. When the risks of medicines are weighed upper to the benefits, the safety information were subsequently proposed to the drug safety advisory subcommittee or related subcommittees and the Drug committee to make decisions for legal strategies to accomplish the aim of risk minimization. For those at lower risk, the information would be distributed by various channels to health professionals.

Since then, the Adverse Drug Reaction Monitoring Center (ADRMC) has established ADR monitoring network in the collaborating hospitals throughout Thailand. The national system for reporting of suspected adverse reactions related to suspected drugs, commonly known as spontaneous reporting system, is currently operated. By the year 1992, nineteen ADRM regional centers were founded according to the organizational structures of reporting network in the hospitals under the health service development network delivery system. At present, 18 centers have been rearranged in 2011. At present, the center has changed its name to “Health Product Vigilance Center (HPVC) according to the extended role to monitor safety of other products within the responsibilty of the ThaiFDA. Additionally, the Thai Food and Drug Administration also initiated post-registration procedures implementing the Safety Monitoring Program (SMP) for new drug registration. This provides databases of new drug safety profiles from the Marketing Authorization Holders (MAHs) for at least two years after conditional drug approval.

All healthcare professionals, especially pharmacists and physicians, are encouraged to send all information about ADRs related to medicines to the national center for pharmacovigilance (NPVC). Initial reports should include the following minimum information: an identifiable patient, a suspected drug, an identifiable data providing source, an event or outcome with suspected causal relationship. Fatal or life-threatening event requires immediate reporting to the NPVC (e.g. by telephone, fax, or e-mail) or within 48 hours. Suspected unexpected /unlabeled serious adverse reactions (SUSARs) require reporting within 15 calendar days, and for serious, but labeled or other non-serious symptoms require reporting within 2 months. In addition, online individual case reporting system was initiated and will be functioned in January 2010.

The main roles of the national center for pharmacovigilance (NPVC) are:

1) to collect and analyze individual case reports of ADRs with causality assessment

2) to generate new signals from all information of drug-related adverse events

3) to communicate the statistics of the reported adverse events, either known or previously unobserved

4) to identify risk factors or related factors influencing to adverse events

5) to conduct risk evaluation and epidemiological studies in cooperation with the relevant committee and /or subcommittee to make more informed regulatory decisions based on benefit-risk analysis

6) to alert prescribers, pharmaceutical industry, and the public about safety signal of adverse reactions.

From the NPVC's roles, the important elements of pharmacovigilance activities at national level could be summarized as:

(1) Data management of individual case reports of ADRs

(2) Signal detection, risk identification and risk assessment

(3) Making decisions for risk minimization tools or strategies

(4) Risk communication and implementation of risk minimization actions

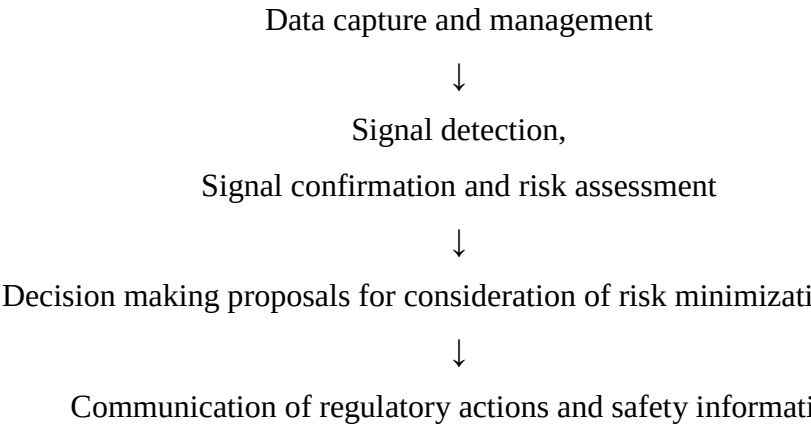

Figure 2.3: Pharmacovigilance activities within the HPVC

From figure 2.3, pharmacovigilance activities within the HPVC comprise 4 main elements. In order to understand the organizational functions clearly, the operational procedures of each elements are briefly described below:

1) Data management of individual case reports of ADRs

The reports of suspected drugs related to adverse reactions from various sources in the country sent to the NPVC will enter into the Thai Individual Case Safety Report (ICSR) database, called ThaiVigiBase. Data in each report will be keyed in and screened by minimum criteria for essential requirement of data element. Verification of ICSR data will be done in order to ensure the storage of cleaned database. Annual summary of ADR reports will be prepared and disseminated to various stakeholders. In addition, information of drug safety from secondary sources such as DRA or mass media e.g. BBC, CNN, etc are also daily monitored.

2) Signal detection, risk identification, and risk assessment

For signal detection, the Reporting Odds Ratio (ROR), a measure of disproportionality, is used to highlight drug-ADR pairs appearing in ThaiVigiBase more frequently than expected. An automated technique is used every 6 months to examine ThaiVigiBase for new signals. Subsequently additional triage criteria are applied and utilized as signal screening tool.

Drug-ADR pairs selected by the automated method and subsequently screened by triage criteria will be judged as potential signal. Those potential signal lists will be determined by the signal review panel whether safety issues are significantly vital for detailed review. The detailed review process involves consideration of the clinical significance of the individual case safety reports, along with a review of relevant literature. Subsequent signal strengthening process may be conducted if clinical review indicates significance of safety issue.

3) Decision making procedure to consider risk minimization tools

Decision making proposals will be processed through the drug safety advisory subcommittee’s meetings, using many kinds of relevant information from various sources, including “Signal” and/or safety information from ThaiVigiBase. Risk

minimization strategies will be proposed to the national drug committee to make final decision.

4) Risk communication, and dissemination of risk minimization tools

The NPVC carries out various kinds of media to communicate safety information. The *Medical and Health Product Bulletin* is issued quarterly. It includes the latest news on health product knowledge and risk, including a case report column and regulatory information. The Bulletin is done via the Bulletin working group, in order to determine subject, content, and format of each periodical. Other publications are occasionally arranged due to safety issue occurrences such as *Safety News*, distributed to all healthcare professionals, especially when there are serious or emergency drug safety issues, *Annual publication* of the previous year's ADR reporting. *Manuals and guidelines*, describing the work of the NPVC and the SOP in ADR reporting are provided and periodically reviewed. *Group email*, communicating with all members of the network nationwide, and HPVC *homepage*: www.fda.moph.go.th/vigilance are also initiated and operated.

2.1.5 Relevant literature review in pharmacovigilance indicator development

An internet search on the terms 'pharmacovigilance indicators' gave around 83 hits and only 39 hits, both English and non-English version, were directly related to pharmacovigilance. The search illustrated the lack of a set of comprehensive indicators for pharmacovigilance both at system level and at the organizational level. "Regulatory pharmacovigilance seems to have received more attention in terms of indicator development (the SPS report, 2009)". This could be seen in the study of WHO, *Effective drug regulation; A multicountry study*, conducted by Ratanawijitrasin et al. (2002). The study recommended two parameters to analyze the performance of an ADR reporting system. They are "*the ratio of the average number of ADR reports to the number of physicians and pharmacists*; and *the ratio of the average number of ADR reports to the number of drugs registered in each of the countries* (Ratanawijitrasin et al., 2002)". The report mentioned the rationale for these

parameters that a sufficient number of reports, as well as better and complete information from reports received could help generating signals as soon as possible. In addition, the participation of health professionals is also an important factor that increases awareness in ADR reporting system and would encourage reportings from various sources.

In 2004, the WHO Immunizations, Vaccines, and Biologicals program for strengthening national regulatory authorities recommended 8 indicators for post-marketing surveillance of adverse events following immunization (AEFI). All of them were qualitative / structure indicators. “They were 1) *Guidelines and a procedure* for monitoring and management of AEFI; 2) *Roles and responsibilities of the key players* clearly defined and documented; 3) Routine *training/information* on AEFI monitoring and management provided to health staff; 4) Routine & functional system for regular *review of safety and efficacy for regulatory action*, including a process to review and *share relevant data* between key players; 5) *System for providing feedback* on AEFI from the national to all levels; 6) Capacity to *detect and investigate* significant vaccine safety issues; 7) Documented *process for action* to be taken regarding vaccine performance; 8) Provision for post-marketing safety monitoring *in the MAH* process (WHO-AEFI, 2004)”.

According to compulsory regulatory pharmacovigilance in Thailand, Amrumpai et al. (2005 & 2007) described the process for indicator development of the safety monitoring program (SMP) that aims to monitor safety information of those registered as new medicines. The indicators were broadly drug safety–specific indicators that were identified through the structure, process, and outcome model. The indicators were developed through a three-round modified Delphi method, including semistructured interviews, mailed questionnaire, telephone recall, and in-person contact. “Seventy-one indicators were identified in the first round, 40 indicators in the second, and 36 indicators in the final round, and then the indicators were regrouped into 19 safety indicators (Amrumpai et al., 2005)”. “Nine core structure indicators were grouped into 4 domains: *Policy, law, regulations, and guidelines*(3); *Organization*(1); *Personnel*(4); and *Information system*(1). Six core process indicators

were grouped into 3 domains: *Evaluation process for application* to the SMP(1); *ADR management system*(3); and *Evaluation process for releasing* from the SMP(2). Four core outcome indicators were grouped into 1 domain namely *Safety indicator*. For ADR management system, this domain comprises 3 process indicators: 1) *Validity in ADR reporting* from health professional; 2) strictly performing in *collecting ADR of drug company*, and 3) ADR management system: *ADR detection, ADR assessment, ADR minimization, and ADR communication* (Amrumpai, 2005)".

The report *Assessment of the European Community System of Pharmacovigilance*, which was called the Fraunhofer report (2006), provided many useful comprehensive lists of PV indicators. The indicators were developed from a literature review and from interviews of the European regulatory agencies. In that report, PV functions were divided into six phases: 1) Data collection, 2) Data management, 3) Signal detection, 4) Safety issue assessment, 5) Decision making, and 6) Communication and action. The assessment of the European PV system was based on a systematic analysis of "processes, stakeholders, resource availability, functional capability, gaps, strengths and weaknesses, and best practice (the Fraunhofer report, 2006)". The indicators were distinguished into input, process, and output indicators. The Delphi group was asked to determine the candidate indicators "according to their relevance, practicability, and interpretation (the Fraunhofer report, 2006)". The Fraunhofer report finally selected the performance indicators grouped under the following headings: "*data collection, data management, signal detection, safety issue assessment, decision making, communication/action, and general factors* (the Fraunhofer report, 2006)". The critical success factors were also identified through the Delphi method.

Some relevant indicators were also identified from the guidance document *Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries*, submitted to the USAID by the Strengthening Pharmaceutical Systems (SPS) Program under Management Sciences for Health (MSH). The SPS report (2009) presented that the Indicator-Based Pharmacovigilance Assessment Tool (IPAT) was developed as a comprehensive performance metric for

pharmacovigilance and medicine safety systems. The first list of candidate indicators was assessed “using explicit criteria for objectivity, reliability, relevance or adequacy, measurability, validity, and practicability (the SPS report, 2009)”. The candidate indicators were determined in three rounds of Delphi consultations and the iterative process was conducted to explore the opinions of experts. The indicators recommended by the Delphi group were used to formulate the relevant assessment questions. After that, pilot-testing in Rwanda and evaluating the indicators for relevance and feasibility in South Africa were carried out. Finally, feedback from the pilot testing was used to further refine the tool that was also reviewed by three external consultants. “The IPAT consists of 43 indicators—26 core and 17 supplementary—that address five pharmacovigilance and medicine safety system components: 1) *Policy, law, and regulation*; 2) *Systems, structures, and stakeholder coordination*; 3) *Signal generation and data management*; 4) *Risk assessment and evaluation*; and 5) *Risk management and communication* (the SPS report, 2009)”. The indicators are also classified by “structure”, “process”, or “outcome” according to the objects they measure.

Recently, the WHO Programme for International Drug monitoring has initiated a nearly completed list of performance indicators for pharmacovigilance. The final list of potential indicators would be determined by peer review before accepted by the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) (Edwards and Isah, 2011). The initial report showed that “the indicators would be measures of inputs, processes, outputs, outcomes, and impacts for development projects, programs, or strategies, as well as describe how well a PV program is achieving its objectives (Edwards and Isah, 2011)”. The indicators themselves must have the following attributes: “easy to measure, understand and interpret as well as inexpensive to obtain; not require too high a level of expertise to use; reproducible; sensitive enough to detect PV problems needing attention; and sufficiently robust to serve as an efficient monitoring tool (Edwards and Isah, 2011)”. Each individual indicator have to meet their inclusion criteria as an indicator by the followings: “the content, purpose and scope of the indicator, and the definitions of key terms; what it will measure and why it is important; sources and methods of data collection and

indicator calculation; how the results can be interpreted; and what are the limitations of the indicator (Edwards and Isah, 2011)".

2.2 Models for organizational assessment and evaluation

Evaluation is the systematic determination of value, and importance of something or someone using criteria against a set of standards. Assessment is sometimes used interchangeable with evaluation by making no judgments on the measurements. Organizational or program evaluation is a set of activities and techniques to determine how an organization or a program is operated. It could involve quantitative methods or qualitative methods or both of them. Several dimensions of the goals, processes, and outcomes of the organization's work could be assessed, for example:

1) **Need assessment** identifies the volume and severity of the problems that the organization has to address. It includes the analysis in order to know the people whom the problems may affect, the magnitude of the problems, and the impacts that may emerge from the problems.
2) **Program theory** may be called a logic model or impact pathways. Program theory breaks down the work components of the organization and indicates the expected effects. An analysis of the organization by program theory identifies the desired outcomes based on how the organization is managed. It could also analyze the unexpected consequences that may emerge, both positive and negative. The program theory leads to the hypotheses for impact analysis.
3) **Process analysis** determines how the organization is being managed. This method can be viewed as **formative approach** which demonstrates whether the organization is performing as intended. An effective organization may produce the desired results if its work processes is managed properly. Thus, this part of the evaluation focuses on the process. Its main purpose is to identify deficiencies so that the improvement strategies would be applied.
4) **Outcome evaluation** may sometimes be called **summative evaluation**. This is a method of judging the final consequences of the activities. The method

focused on the results of the project, program or the organization. It may include short-term and long-term outcomes.

5) **Impact evaluation** analyses the causal effects of the organizational work. It could be seen as the most difficult part of the evaluation. The aim of this method is to determine whether the work of the organization is causing either the anticipated or unanticipated impacts.
6) **Cost-benefit or cost-effectiveness analysis** assesses the efficiency of the organization. The benefits and costs of the organizational activities are determined for comparison. Efficient organizations refer to those that have a lower cost comparing to the benefit.

2.2.1 Approaches for organizational performance improvement

An approach in developing performance measures is needed to help accomplishment of multiple goals and services of a governmental agency. Performance measures would be a management tool to develop a strategic plan, to serve the different and changing needs and expectations of various stakeholders, and also to decrease the conflict of interests among various groups in the complex society. Many organizations have adopted one of the performance improvement models or tools in order to help them manage effectively. There are a lot of approaches or tools available on the shelf, although it is difficult to select the appropriate one. These approaches provide a holistic framework to help the organization to design for the organizational assessment and enhance the agency to fulfill its goals. Some of the popular performance improvement models and tools are briefly described below:

1) **Balanced Scorecard** refers to a combined multi-dimensional framework for managing the organizational objectives, targets and performance measures across key corporate perspectives. 4 main perspectives are recommended for every organization to be assessed: 1) *financial perspective* such as profitability; 2) *customer perspective* such as stakeholder's satisfaction; 3) *internal process perspective* such as response time, quality and cost of interventions; and 4) *learning and growth perspective* such as employee satisfaction, and information system.

2) **Business Process Reengineering** is an approach to review and redesign the organizational processes in order to improve performance in terms of cost, quality of service and timeliness. The example of the organization that has adopted this tool is the Thai Farmer Bank.

3) **ISO Quality System** refers to the global standard and approach for quality management systems. The approach focuses on the management of processes and documentation in order to meet customer needs or stakeholder expectations. Various industries have adopted this tool for their organizational development.

4) **Six Sigma** is an adapted engineering analysis for process improvement based on data analysis to identify sources of performance variation and the collective ways. It emphasizes on improving system performance and decreasing process variability by removing defects and their causes. The general approach to apply the Six Sigma methodology follows the steps called DMAIC: Define, Measure, Analyze, Improve, and Control. The *Define* phase refers to the identification of the critical elements of a process for quality control. The *Measure* phase aims to identify the capability of the current organizational structure and provides a baseline performance standard. After the baseline performance is defined, the *Analyze* phase identifies areas of highest process variability and the potential causes. The *Improve* phase is then performed, emphasizing on the solutions to decrease the variability of a process in the existing system. After an improved process is accomplished through an iterative process, the *Control* phase focuses on the abilities to maintain these improvements. The final step also involves the followings of other problems that may emerge from the new system. The organizations that have adopted this tool to improve their performance such as the Toyota Motor company, the Motorola company.

2.3 Organizational performance assessment

2.3.1 Overview the concept of organization and its performance

"An organization is made up of people working together toward a shared goal (Lusthaus et al., 2002)". Organizational goals make organizations different from other groups of people in the society such as families, communities or states. Organizations could be mainly distinguished, according to their objectives, into public and private enterprises. The organizations are viewed as open systems. This means that the organizations always interact with external forces. They are expected to conduct complex tasks in order to respond to a complicated changing environment. The success or failure of an organization depends on these socially interactive practices. Any organization consists of independent groups that have different goals, thus, different agencies have their own ways or work processes to accomplish its multiple goals. In the changing environment, systematic examination is important for better understanding the enabling factors or the obstacles to improve the organizational performance.

There are many approaches to assess the performance of an organization. In the 1940s, concepts of effectiveness and efficiency were determined as the major aspects of the performance. It was perceived that an organization was performing well if it could accomplish its expected goals (effectiveness) or if it used relatively few resources comparing to the results achieved (efficiency). Good performance means the organizations are performing to meet their intended goals and practicing within the reasonable resource parameters (Campbell, 1970, cited in Lusthaus et al., 2002).

During the 1950s and early 1960s, it was believed that the most successful organization had to be designed in the bureaucratic form (Weber, 1947, cited in Lusthaus et al., 2002). "The assumption was that the more bureaucratic the organization, the better performing and efficient it would be (Lusthaus et al., 2002)". The government and private agencies determined their performance against the Weber's criteria for bureaucracy that were specialization, formalization and hierarchy.

The assessment focused on the bureaucratic components when diagnosing the organizations (Blau and Scott, 1962; Hickson and Pugh, 1995, cited in Lusthaus et al., 2002).

During the 1960s and 1970s, most of the organizations started to find new ways to assess their performance. Organizational assessment became more complicated, trying to integrate as many aspects of an organization as possible (Levinson, 1972, cited in Lusthaus et al., 2002). A variety of rigorous cost accounting tools and techniques were initiated by system analysts to help understand financial performance. These included planning programming budgeting systems (PPBS) and zero-based budgeting. At the same time, human related factors such as problem solving approach or teamwork concept, were also identified by social scientists.

In the late 1970s and 1980s, many new approaches to identify the success or failure of the organization have emerged. Stakeholders became one of the important factors that have to be explored in the assessing process (Peters and Waterman, 1982; Walton, 1986, cited in Lusthaus et al., 2002). By the 1990s, more holistic and comprehensive tools to describe the organizational performance and the factors related to it in any types of organizations were clearly demonstrated (Harrison, 1987; Osborne and Gaebler, 1992; Scott and Meyer, 1994, cited in Lusthaus et al., 2002).

2.3.2 Logical framework for organizational assessment

The organizational assessment model presented below is a diagnostic tool borrowed from the model of Lusthaus et al. (2002). It aims to assist the organizational performance assessment and help identify the relevant uncertain aspects in the organization that might affect its performance in the future. It is a general framework that is useful to analyze any types of the organizations. The framework also reflects the determination of how well the organization performed its work, and how well it is performing within its particular environment.

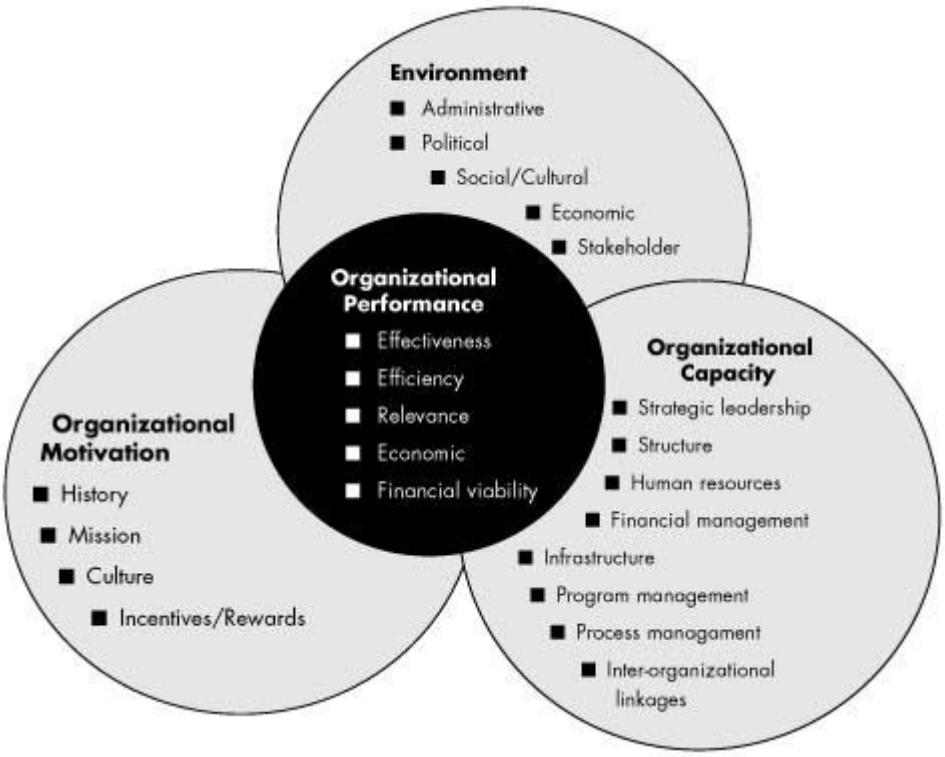

Figure 2.4: Logical framework for organizational assessment (Lusthaus et al., 2002)

From figure 2.4, organizational performance comprises four main aspects: effectiveness, efficiency, ongoing relevance and financial viability. It should be noted that economic aspect of the performance, depicted in the figure, was not explained in the textbook. The framework implies that performance is driven by the particular external and internal forces: organizational capacity, internal motivation, and its external environment.

"The framework views organizational performance as a function of its enabling environment, capacity and organizational motivation (Lusthaus et al., 2002)". Table 2.1 below illustrated the definition of each aspect and examples of the indicators derived from the framework.

Table 2.1: Definition of each aspect in the framework for organizational assessment

Organizational assessment framework	**Definition (Lusthaus et al., 2002)**	**Example of indicators / areas to be examined (Lusthaus et al., 2002)**
1.**Organizational performance**	Results of an organization's work on how well or badly the organization does for a particular job or activity	
1.1 Effectiveness	The ability of an organization to successfully meet its objectives or purpose	Achievement of goals / Number of clients served / Service access and usage / Knowledge generation and utilization / Quality of life changes
1.2 Efficiency	The ability of an organization to maximize the use of its resources to reach its purpose	Output per staff / Overhead per program costs / Timeliness of service delivery / Cost per client served
1.3 Relevance	The ability of an organization to satisfy stakeholder requirements, or to respond to external forces	Stakeholder satisfaction / Changes in reputation among key stakeholders / Number of supporters, subscribers, funders
1.4 Financial viability	The ability of an organization to generate and manage adequately its resources in order to ensure its ongoing existence	Return on investment / Profitability / Percentage of funding by source

Organizational assessment framework	**Definition (Lusthaus et al., 2002)**	**Example of indicators / areas to be examined (Lusthaus et al., 2002)**
2.**Organizational capacity**	The ability of an organization to use its resources to perform its work	
2.1 Strategic planning / leadership	*Strategic planning* refers to the pattern of calculated responses to the environment, including resource deployment, that enable an organization to achieve its goals. *Leadership* is basically the process through which leaders influence the attitudes, behaviors and values of others towards organizational goals.	*Strategic planning* Is there a formal or informal organizational strategy? / Is the strategy supporting a high level of performance? / Is there a process for clarifying and revising the organization's strategy? *Leadership* Do people in the organization support formal leadership? / Does all staff have an opportunity to suggest changes in the organization?
2.2 Structure	The ability of an organization to divide labor and assign roles and responsibilities to individuals and groups in the organization, as well as the process by which the organization attempts to coordinate its labor and groups.	Does the governing structure have a clearly defined way to review and set organizational direction? / Are the organization's mission and goals supported by its structure? / Are roles within the organization (groupings as well as individual) clearly defined? / Are work processes clear and adequately structured?

Organizational assessment framework	**Definition (Lusthaus et al., 2002)**	**Example of indicators / areas to be examined (Lusthaus et al., 2002)**
2.3 Human resources	*Human resources planning* involves forecasting the human resources needs of the organization, and planning the steps necessary to meet these needs. *Staffing* an organization means searching for, selecting and orienting individuals who have the appropriate range of knowledge, skills, behavior and values to meet the organization's needs. *Developing human resources* in an organization means improving employee performance by increasing or improving their skills, knowledge and attitudes.	To what extent does the organization's ability to plan for its human resources needs affect its performance? / To what extent does the organization have adequate staffing procedures to ensure that it knows the type of staff required for high performance? / Does the organization have a training and development policy? / Can and does the organization assess training and its effect on performance? / Staffing procedure / day-to-day functions / work-hours / skill / knowledge / attitude / training
2.4 Financial management	Planning, implementing, and monitoring the monetary resources	Is regular and periodic financial planning undertaken to support performance? / Is there adequate budgetary planning? / Are budget plans timely?
2.5 Infrastructure	The basic conditions (facilities, technology) that allow an organizational work to proceed	Adequate lighting / Clean water / Computer / IT

Organizational assessment framework	Definition (Lusthaus et al., 2002)	Example of indicators / areas to be examined (Lusthaus et al., 2002)
2.6 Program management	The ability of an organization to carry out its institutional role	Are program and project plans linked to the organizational mission? / To what extent does the organization appropriately implement its programs? / To what extent does the organization monitor its programs appropriately? / Are there adequate opportunities to clarify roles and responsibilities? / Are there adequate opportunities to review program indicators to measure progress against plans?
2.7 Process management	The ability of an organization to manage the organizational work	Is enough information available on all alternative courses of action? / Is the process of planning contributing to the strategic direction of the organization? / Do plans provide adequate direction to organizational members? / Are plans, policies and procedures generally followed? Why or why not? / Do staff members receive information related to the organizational mission and progress in fulfilling the mission? / Is adequate monitoring and evaluation occurring to improve performance?

Organizational assessment framework	**Definition (Lusthaus et al., 2002)**	**Example of indicators / areas to be examined (Lusthaus et al., 2002)**
2.8 Inter-organizational linkages	The ability of an organization to manage its external relationships	Are external linkages adequately established or pursued to support performance? / Is the organization communicating information about its work to external stakeholders, including the general public? / Are external technological linkages adequately established or pursued to support the organization's performance? / Do electronic networks effectively respond to the needs, shared interests and capabilities of the organization?
3.Organizational motivation	The driving forces behind the organizational personality	
3.1 History	The story of an organization's inception, growth, awards, achievements, and notable changes in structure or leadership, as well as its failures and near misses	Assessment of date and process of founding / Awards / Struggles / Changes in size, program, leadership
3.2 Mission and vision	An expression of how people see the organization operating	Mission statement / Goals / Role of mission in shaping the organization and giving purpose and direction

Organizational assessment framework	Definition (Lusthaus et al., 2002)	Example of indicators / areas to be examined (Lusthaus et al., 2002)
3.3 Culture	Set of values, guiding beliefs, understandings and ways of thinking that are shared by members of an organization and are taught to new members. Culture represents the unwritten, informal standards of an organization.	Attitude about working, colleagues, clients or stakeholders / Underlying values, beliefs, norms
3.4 Incentives / Rewards	The reason for staff to join an organization, and the way an organization rewards and punishes its staff	Motivation / Stimulation / Autonomy / Intellectual freedom / Career path / Peer recognition / Prestige
4. Environment	The factors that affect the organization to survive and perform well	
4.1 Administrative / Legal	The formal rules within which the organization operated / the ability of an organization to develop and enforce laws and policies	Is the organization's legal framework clear? / Is the legal framework consistent with current practice? / Is relevant legislation up to date? / Is the organization affected by a regulatory framework?; by a public service commission?; by global and regional agreements and standards?
4.2 Political	The ability of an organization to organize civil society among other groups	Are there government policies and programs supporting the organization? / How responsive is the government system to the organization's needs and issues? / Degree of transparency / Knowledge of the electorate

Organizational assessment framework	Definition (Lusthaus et al., 2002)	Example of indicators / areas to be examined (Lusthaus et al., 2002)
4.3 Social / Cultural	The ability of an organization to shift social and cultural attitudes	Do prevailing social and cultural values support the organization's work? / Is the organization affected by Religious/ethnic/gender/class customs and biases? / Cultural values/norms? / Violence and crime? / Cultural behavior?
4.4 Economic	The ability of an organization to develop competition policy framework and manage in the situation of resources constraint	Does economic policy support the organization's ability to acquire technologies and financial resources? / Is money available to do work? / Is the budget allocation adequate for the organization's work? / Is the economic growth rate supportive of development? / Are there supportive monetary and fiscal policies (including interest rates)? / Level of competition
4.5 Stakeholder	The ability of any group within or outside an organization that has a stake or influence in the organization's performance.	Creditors / Suppliers / Employees / Owners

According to the table 2.1, details of each broad area for organizational assessment were briefly described as the followings:

1) Organizational performance

Most non-profit organizations assess their performance in terms of how well they meet their mandates and the ability to fulfill their stated mission, purpose or goals. Effectiveness and efficiency have been the standard concepts used for determining the organizational performance. However, many new ideas derived for assessing the organizational performance have evolved, including adaptability and change management. Many of these ideas support the organization to be able to survive and perform well. The logical framework identified four key elements of organizational performance: *effectiveness, efficiency, relevance and financial viability.* Others may classify the elements of performance with different terms. But it is obvious that all types of the organizations try to manage the various elements of their performance in balance (Lusthaus et al., 2002).

Performance measurement has been developed during the past several years. In the 1950s, performance was referred to "the *extent to which an organization as a social system fulfilled its objectives* (Georgopoulos and Tannenbaum, 1957, cited in Lusthaus et al., 2002)". In the 1960s and 1970s, performance is defined as "*the ability of an organization to exploit its environment to access scarce resources* (Yuchtman and Seashore, 1967, cited in Lusthaus et al., 2002)". In the 1980s and 1990s, constructivists identified organizational goals in a more complex concept than the existed organizational theory. However, performance was commonly determined at four levels (Lusthaus et al., 2002):

- The individual employee (performance appraisal)
- The team or small group (team performance)
- The program (program performance)
- The organization (organizational performance).

In the above framework, the concept of overall organizational performance was remarked as the combination of individual, team and program performance. There are traditional approaches that lead some direction in understanding the performance. For example, health ministries may measure their performance in terms of the patients who received care and treatment, education ministries may measure the number of children who went to school for learning. Energy companies may measure performance in terms of electricity supplied for the communities. Municipalities may use the quality of life of their citizens, while the private sector may use profitability as the performance measure.

"A measurement of organizational performance needs to involve the perceptions of the organization's multiple stakeholders, including those who work within the organization (Hassard and Parker, 1993, cited in Lusthaus et al., 2002)". Each interest group or stakeholder in an organization may have a different concept of good performance. For example, "the customers of a hydroelectric plant want reliable electrical service, while the government wants to reduce its subsidies to the plant. In research centers, researchers might define performance in term of the number of published articles, while senior administrators might define it as the quantity of accessed grants taken to the research center (Lusthaus et al., 2002)".

The framework above integrated the various concepts into a multi-dimensional framework for understanding the organizational performance. It is seen to be suitable for any types of organizations. This study was employed the concept of two main elements: *effectiveness and efficiency* in assessing the organizational performance.

Effectiveness

"Any organization is set up for a particular function that is clarified through its goals (Lusthaus et al., 2002)". Specifically, organizational effectiveness is defined as *the extent to which an organization is able to fulfill its goals*. In assessing the effectiveness of an organization, it should be firstly explored the functional purposes of the organization. The functional purposes lead to better understand the dimensions

of the organizational effectiveness. The dimensions of organizational effectiveness could be defined as the perspective of the role in achieving the organizational goals (Lusthaus et al., 2002). However, various stakeholders perceived the dimensions of effectiveness differently (Wohlstetter, 1994, cited in Lusthaus et al., 2002). For example, "profitability means different things to different stakeholders. To a worker, it might mean expected wages with an agreement that leads to long-term employment. To a manager, profit might mean an incremental salary. To an investor, it might mean better returns on investment (Lusthaus et al., 2002)".

Assessing Effectiveness

In assessing the effectiveness of a governmental agency, it should be started from identification of its goals. The organizational goals can be identified through various organizational documents such as the organizational plan or strategy, and the legislation document for organizational establishment. Mission statements can also be a specific source of information about the organizational purpose and goals. After the organizational goals are recognized, a set of measurement questions can be designed. The measurement questions could range from very broad to very specific questions. At the final step, the potential indicators can be formulated (Lusthaus et al., 2002).

Indicators of Effectiveness

In general, it is impossible to have a list of indicators that can be used for every organization (Eimicke, 1998, cited in Lusthaus et al., 2002). Some examples of the indicators to assess the effectiveness are as the followings: achievement of goals, number of clients served, service access and usage, quality of life changes, etc (Lusthaus et al., 2002).

Efficiency

Another important concept for determining the organizational performance is efficiency. Efficiency refers to the measurement of the organizational outputs

obtained compared to its resources used. More specifically, “efficiency is defined as *a ratio that reflects a comparison of outputs accomplished to the costs incurred for accomplishing these goals* (Lusthaus et al., 2002)”. “The question of efficiency is how economical the organization has been producing the outcomes (Barker, 1995, cited in Lusthaus et al., 2002)”. It could be implied that “efficiency is achieved when the minimum level of resources is used to produce the target output. For example, many educational organizations use cost per graduate as an indicator of efficiency. Conversely, they use repeater and dropout rate as a sign of inefficiency (Lusthaus et al., 2002)”. Moreover, another approach to assess the organizational efficiency is “a measure of how well the organization is managing its strategy policy, procedure and work processes (Lusthaus et al., 2002)”. For example in the private sector, especially in the manufacturing settings, re-engineering of the production process was adopted to improve its efficiency (Lusthaus et al., 2002).

Assessing Efficiency

It is difficult to assess the organizational outputs, especially in service organizations. “Even in organizations that produce tangible products, it still may be difficult to obtain a timely and ideal assessment of output that includes quality measurements over time or across firms (Bowles and Coates, 1993, cited in Lusthaus et al., 2002)”. For example, the efficiency of a research institute is commonly measured in term of the number of research papers published per the number of researchers. The question of the quality of those papers has been raised. Thus, in order to assess the quality dimension in an efficiency indicator, output can be measured in term of the number of research articles published in famous journals (Lusthaus et al., 2002).

Indicators of Efficiency

There are some examples of preliminary indicators that can be used to guide an assessment: cost per service provided, outputs per staff, cost per client served,

employee absenteeism and turnover rates, timeliness of delivery of services, etc (Lusthaus et al., 2002).

In summary, efficiency and effectiveness are traditional concepts used by organizational assessors to evaluate performance. An organization is efficient if its outputs obtained are relatively high comparing to the resources used. It is effective if it achieves its intended purpose or goals. However, "organizations can be highly effective without being efficient, and can achieve relatively high levels of efficiency without being effective (March and Sutton, 1997, cited in Lusthaus et al., 2002)".

Other two aspects of organizational performance were briefly described as the followings:

Relevance

The performance of an organization should accomplish the needs and expectation of various stakeholders. An organization must receive supports from its environment in order to survive and perform well. "The ongoing relevance of an organization is defined as *the ability of an organization to meet the needs and gain the support of its priority stakeholders in the past, present and future* (Lusthaus et al., 2002). "Organizations that survive are those that learn on a continuous basis and use the learning acquired to improve and perform (Senge et al, 1999, cited in Lusthaus et al., 2002)". Clients and customers are the key stakeholders influencing the performance of any organization. At present, private agencies devote their efforts to identify customer reactions to new products or services. At the same time, they recognize the government as an important stakeholder in their businesses. The government agencies also recognize their relevance to other agencies. Thus, both groups of organizations increase awareness on the needs and expectation of their stakeholders.

Some examples of preliminary indicators for relevance are shown as the followings: stakeholder satisfaction (clients, international institutions, donors, etc.),

changes in partner attitudes, changes in organizational reputation among key stakeholders, etc (Lusthaus et al., 2002).

Financial viability

Financial viability refers to the ability of the organization to generate the resources it requires. This concept is easily noticed in the private sector, but less in the organizations supported by taxpayers. Specifically, financial viability refers to *"the ability of an organization to raise the funds required to meet its functional requirements in the short, medium and long term* (Lusthaus et al., 2002)". There are three dimensions in assessing the financial viability of an organization. "The first relates to *the ability of an organization to generate enough cash to pay its bills and profitable* (Lusthaus et al., 2002)". "The second dimension of assessing financial viability deals with *the sources and types of revenues on which the organization bases its costs* (Lusthaus et al., 2002)". "The third dimension is *the ability of an organization to live within its allocation.* This dimension focuses on the actual ability to manage a budgeting process, as well as the results of the process (Lusthaus et al., 2002)".

Governmental agencies must manage their resources efficiently in order to convince the budgetary authority to support more grants in the future, while private organizations must manage cash, accounts receivable, and accounts payable. The starting point in assessing financial viability is to review the organization's financial statements including income and expense statements, balance sheet and cash flow statements (Lusthaus et al., 2002).

Some examples of preliminary indicators for assessment of financial viability are shown as the followings: ratio of current assets to current liabilities, ratio of total assets to total liabilities, growth indicators in terms of number of funders, amount of resources mobilized, assets, capital, revenues, etc (Lusthaus et al., 2002).

Other areas of organizational assessment; organizational capacity and motivation, and environment were briefly described as the followings:

2) Organizational capacity

Organizational capacity is the ability of an organization to use its resources to manage its work. The assessment of organizational capacity involves all of the resources used, as well as the supportive systems and processes to develop its work. Performance is affected by organizational capacity in seven basic dimensions: strategic leadership, human resources, financial resources, infrastructure, program and process management, and inter-institutional linkages. Each of these seven dimensions may be explained in sub-components. For example, the organization's strategic leadership may refer to its structure, governance, leadership, strategic plans and niche management.

Within the above framework, the systems and management practices linked to *human, financial and infrastructure resources* assist the understanding of resource management. *Strategic leadership* involves the strategies that lead the direction of an organization. *Strategic planning* refers to the set of activities intended to respond to the changing environment, including resource deployment that enable an organization to achieve its goals. *Program management* refers to the ability of an organization to carry out its institutional role. *Process management* examines the way the organization manages its human relationships and the interactions of work processes. *Structure* identifies the links between how an organization is operated and its mission, as well as the roles of human and financial resources that play in daily activities. Finally, *inter-institutional linkages* refer to the ability to manage the relationships, partnerships and alliances with other organizations.

3) Organizational motivation

Within an organization, organizational motivation represents the underlying personality of the organization. It refers to the organizational culture, history, mission,

values and incentive systems. These factors affect the organizational performance in terms of quality of work, quality of decision making processes, and the degree of participation of internal stakeholders. The motivation drives the staff of the organization to perform its roles and responsibilities.

Within the framework, organizational motivation has been assessed by analyzing a number of organizational dimensions; organizational history, culture, incentive and reward system, as well as its mission and vision. *History* refers to the assessment of how and why the organization got established. It includes date and process of establishment, important awards/achievements, struggles, and changes in size, program management, or leadership. In the similar way, the assessment framework also explores the organization's mission, values and vision in order to understand the driving forces behind its performance. *Mission and vision* include the evolution of mission statement, goals, role of mission in driving the agency's purpose and direction. *Culture* involves attitudes about working, colleagues, clients or stakeholders, underlying values, beliefs, and norms. *Incentive and reward system* include motivation, stimulation, autonomy, intellectual freedom, remuneration, grant access, career path, peer recognition, and prestige. Taken together, these factors lead the organization to its personality and affect its performance and quality of work.

4) External environment

Since organizations are viewed as open systems, the external environment affected much in their management. Organizations exist within the particular external contexts that facilitate or inhibit their performance, thus, they need supportive facilities from their environment to survive and perform well. The environment leads to determine the level of resources available and the approaches that an organization can employ to carry out its activities. The quality of the environment—such as poor infrastructure in terms of information technology, computers both hardware and software, fax machine, and phone lines—can also inhibit good performance. Thus, in assessing an organization, it should be paid attention to policy or regulatory

environment, as well as economic, political, socio-cultural, environmental, demographic and technological conditions.

From the logical framework, the enabling environment is composed of the administrative or legal, political, economic, socio-cultural, and stakeholder factors. *Administrative or legal* refers to changes in the governmental administrative, as well as legislative policies that are identified and described the official regulations that affect an organizational management system. Administrative or legal factor also refers to the ability of the organization to develop and enforce laws and policies. *Political* dimension examines the ability of an organization to manage each stakeholder's needs and expectations among other groups'. The examples of indicators for exploring political factors are knowledge of the electorate and degree of transparency. *Technology* refers to product development, or R&D capability. *Economic* dimension explores the ability to manage the changing competitive policy framework and also examine economic factors both macro- and micro-economic factors. *Socio-cultural* refers to the ability to manage the changing social and cultural attitudes. *Ecological* dimension explores the ability to assess the environmental impact to the organizational performance. *Stakeholder* refers to the ability of groups to influence the assessed organization.

2.4 Three-Stage model for development of performance indicators

The word "indicator" came from the Latin verb **indicare**, which means to indicate, make known, or point out. Most common definitions of "indicator" describe it as a person, thing, or device that measures, records, or declares something. Indicators can be thought of as pieces of information that provide evidence on matters or objects concerned (the INECE, 2008). This study applied the guidance recommended by the expert working group on enforcement and compliance indicators under the International Network for Environmental Compliance and Enforcement (INECE) to use as the developmental process for design and refinement of the indicators. The guidance was produced for the purpose of helping for indicator design

and development through an integrated process comprised three stages; 1) identifying potential indicators and selecting an appropriate combination; 2) developing indicators through designing and testing; and 3) using the indicators to improve program or organizational performance. For each of these stages, the applications should not be used as a step-by-step process, but they are viewed as an alternative process that the organization can choose those appropriate for its specific situation.

Some important processes that were employed as the guidance to establish and develop the set of indicators in this study are briefly described as the followings:

Stage 1: Identifying scope and selecting criteria for evaluating indicators

A. Determine the scope of the indicators

In order to assess the overall performance and improve management of the national pharmacovigilance center, it is important that the indicators need to be comprehensive. "Comprehensive indicators mean the indicators that cover all the elements or framework of the activities that the agency is responsible for (the INECE, 2008)". The indicator developmental processes require the involvement of various stakeholders including many persons in multiple agencies, as well as the collection of data from many sources, and the implementation of a national data system.

B. Apply logic model

Logic models illustrate the graphical pictures of a result chain between resources used, activities undertaken, and the results of those activities (the INECE, 2008). A logic model must show how outputs and outcomes are measured. It includes structural measures that involve the external environment of the organization and its internal factors such as human resources, financial and infrastructure resources, and management system. Process measures include a series of activities related to a result. Output measures refer to the services or products from the organization's work.

C. Select criteria for evaluating potential indicators

Potential indicators need to be evaluated by a set of criteria to determine whether they are practical to be used. The criteria include the relevance of the indicators to provide valid information about the objects that are being assessed. The feasibility of the indicators is an important criterion to determine whether the indicators are easy to be implemented. The balance of the usefulness of an indicator and the cost to implement the indicator should be carefully considered. The table below demonstrated some examples of the selection criteria for evaluating potential indicators and could be used as the guidance to determine the indicators along the developmental process.

Table 2.2: Criteria for using to develop and select the appropriate indicators

Criterion	Description (the INECE, 2008)
Relevant	Connected to goals, objectives, and priorities of the agency and to the needs of relevant stakeholders
Transparent	Promotes understanding and enlightens users about organizational or program performance
Credible	Based on data that is complete and accurate
Functional	Encourages personnel to engage in effective and constructive behavior and activities
Feasible	The cost of implementing and maintaining a measure does not outweigh its value to the organization or program
Comprehensive	Addresses the important operational aspects of the organizational or program performance

Stage 2: Developing common definitions of key terms, searching data sources, and choosing appropriate combination of indicators

A. Develop common definitions of key terms

The key terms in assessing the organization should be defined in order to arrange the assessment concept and provide a framework for stakeholders to

understand the rationale of the indicators. Thus, clear and understandable definitions should be identified and presented to enhance generating a good assessment tool.

B. Inventory existing data sources

This step is to identify whether the existing data collecting system are available to support the developed indicators. There should be a collecting system that promotes timely and accurate data to be analyzed by the indicators. Many important indicators may not be formulated when there is only the existing data available. Thus many indicators, especially outcome indicators, require new data collecting process to support.

C. Select an appropriate combination of indicators

In order to select the appropriate indicators, all aspects of the organizational performance should be considered, especially outputs and outcomes. A combination of output and outcome indicators can be used to identify what types of outputs produce the most effective outcomes. Output indicators should reflect the results achieved by the organizational activities, and identify whether the mission of the agency is being achieved. It should be recognized that intermediate outcomes could be a source of the important indicators because they often display a direct causal link from the activities and the outputs of the organization. Thus, intermediate outcomes should be closely considered in developing the valuable indicators.

Stage 3: Conducting pilot project to monitor and test

The testing step is an important step that aims to determine whether the designed indicators are accurate and reliable. This step includes pilot testing of the indicators, correcting mistakes and refining them, and finally using them as the development tools to improve the organizational performance.

A. Determine how to design and test

One approach for evaluating the designed indicators is to establish teams within the organization to determine and refine the selected indicators and review

relevant data available. Setting up a schedule for testing and implementing the indicators is then carried out. These working groups should involve the added benefit of each staff and the evolving of their sense of ownership about the new indicators.

B. Conduct pilot projects

Pilot projects provide a period of time for indicators to be developed and tested before being fully implemented. This period includes the analysis of data, adjusting or refining the indicators, and correcting mistakes. The phases of implementation and iteratively testing for the full set of indicators may be in the future period. The more time spent in developing them could bring more accurate information.

C. Consult with experts

Expert consultations can be particularly useful when developing a statistically complex measure. Experts in sampling techniques, statistical analysis, and performance-based management can provide useful suggestion and recommendation. They can also be helpful in determining whether the potential candidate indicators meet the predefined criteria.

D. Monitor the design and testing

Monitoring the new set of indicators can help determine whether the particular indicators need to be adjusted, dropped out or added to the implementation plan. Reports of the results of indicator testing need to be disseminated through multiple communication mechanisms based on an effectively ongoing approach. Many steps also need to be undertaken to confirm the quality of the data through a continuously quality control program. A development plan should clearly display the routine practices of the new indicators and it should be disseminated to both internal and external stakeholders as appropriate.

It should be noted that the above practices are best viewed as an alternative that can be chosen according to specific situations, but should not necessary be used as a step-by-step process.

CHAPTER III

METHODOLOGY

The study aimed to develop the set of performance indicators to measure the effectiveness and efficiency of the NPVC in Thailand, and to be used as a future assessment tool to monitor and assess the organizational performance. The overall approach of the study was initiated through cross sectional research design. Various methods were conducted as the tools to collect and analyze data: 1) documentary analysis was conducted to identify scope of the indicators and select the appropriate logic model, and to identify the list of candidate indicators; 2) observation, face-to-face and in-depth interviews were implemented to identify and analyze various opinions of the staff involved; and 3) expert opinions and group discussion for validating the indicators.

The logical framework for organizational assessment as mentioned in the previous chapter (Lusthaus et al., 2002) was employed to use as the conceptual framework for indicator development. Some guiding processes of Three-Stage Model (INECE, 2008) were employed for identifying and developing the performance indicators and measures, regarding the research objective. The applied development process comprised 3 stages as the followings:

***Stage 1**: Identifying the scope of the indicators and applying logic model*

This stage aimed to identify the indicator dimensions or domains, and to apply logic model to explain performance and the enabling factors related to the pharmacovigilance functions of the Thai Health Product Vigilance Center (HPVC). This stage was conducted earlier through various methodological approaches:

1) analysis of scientific literature, reports, studies, and determining the existing activities done at the Thai National Center for Pharmacovigilance (NPVC) in order to identify the scope of the indicators
2) applying logic model to be used as the conceptual framework for indicator development
3) clarification common definitions of key terms
4) formulation of the indicator domains

Since the assessment in this study aimed to investigate pharmacovigilance in the organizational level, theoretical framework for organizational assessment developed by Lusthaus et al. (2002) mentioned in chapter II, was employed to be the conceptual framework for indicator development. Indicator dimensions or domains were broad areas of interest or themes that were designed to capture the organization's purposes and functions. In this study, the indicator domains were formulated from the combination of the modified conceptual framework for organizational performance assessment (Lusthaus et al., 2002), and the main elements of PV functions at the national center that described details in the previous chapter.

In addition, the goals related to effectiveness and efficiency of the NPVC were defined based on the literature and the official declaration for the organization establishment. The interviews with the chief of the unit and some executive staffs of the ThaiFDA (the director and former director of the technical and planning division) were also done, intended to provide any supplement of the list of goals.

Stage 2: *Development of the first and second draft indicators*

This stage was the main method to serve the objective of this study. The purpose of this stage was to develop the indicators for assessing the performance of the National Center for Pharmacovigilance (NPVC) in order to identify of future priorities for performance improvement. This stage included the selection of appropriate combination of the measures, and searching data sources.

The indicator development process in this stage included 1) reviewing the literature to identify indicators and performance measures related to the organizational performance assessment; 2) identifying areas without available indicators related to the scope of the study and initiating the new ones; 3) listing all the determined candidate indicators, adjusting and adopting them to the organizational context; 4) removing some identical, repeated, or similar indicators; 5) generating assessment questions and listing them along with the candidate indicators; and 6) generating a first draft of candidate indicators. In practice, the iterative process for indicator refinement continued until saturated; no more modification. The final revision was determined by the researcher.

The first draft of performance indicators was developed, mainly based on the reviewing of relevant literatures. The literature review of indicators for pharmacovigilance system was conducted as well as the websites of some regulatory authorities, such as the U.S. Food and Drug Administration (USFDA), the European Medicines Agency (EMEA), Australian regulatory authorities, and the WHO-International Drug Monitoring Program (WHO-UMC) website. Specific topics related to pharmacovigilance indicators such as ADR indicators, ADR monitoring assessment, safety surveillance assessment, drug safety monitoring assessment, were reviewed and analyzed. The information gathering, comparing, analyzing, synthesizing, arranging, writing, and reviewing were iteratively conducted by the researcher.

The journals and websites related to management science and organizational management, such as *Evaluation and Program Planning, Journal of Applied Measurement, American Journal of Evaluation, and Evaluation Review* were also reviewed for indicators related to organizational performance using the following key words: organizational performance assessment, indicators for performance assessment, organizational evaluation, and organizational performance measurements.

It could be summarized that input for indicator development came from 3 main sources:

(1) International PV related sources

Various literatures were reviewed and compared, not only those in the field of pharmacovigilance, but also the related fields. However, the comprehensive listing of indicators was mainly from 1) the Fraunhofer report (2006); *Assessment of the European Community System of Pharmacovigilance*, and 2) the report of the U.S. Agency for International Development by the SPS Program (2009); *Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries*.

(2) Domestic PV related sources

Few articles were directly related to pharmacovigilance indicators. The most related indicators was from the report of Amlumpai and colleagues (2007) that developed safety indicators for new drug Safety Monitoring Program (SMP) in Thailand. The report described the development process for safety monitoring program indicators to support the ThaiFDA in the safety monitoring of new medicines. The indicators provided broad-spectrum of drug safety–specific indicators.

(3) Relevant literature review

The related information from the literatures reviewed in chapter II was also included to be the sources of the indicator development.

***Stage 3**: Indicator validation through expert opinions against predefined criteria*

The purpose of this stage was to ensure that the developed indicators reflect the valid picture of the performance of the NPVC. The validating stage included 1) using validating criteria to assess the candidate indicators for relevance, practicable, and interpretable; 2) refining the final set of adopted indicators; and 3) generating the final draft of the indicators and assessment tools.

After a second draft of the set of performance indicators was developed based on the process in Stage 1 and 2, the experts in pharmacovigilance and evaluation areas

were asked to validate the candidate indicators and measures. Since the general criteria for good indicator development that mentioned in the previous chapter were difficult and complex for using, the integrated criteria with some modification were employed from the Fraunhofer report (2006) in order to make the validating process appropriate and better understandable. These criteria comprised 3 dimensions as the followings: relevance, practicability, and interpretability.

Relevance: How was the indicator to display a valid description of the performance of the NPVC in Thailand?

Practicability: How feasible was it to be used as an indicator?

Interpretability: How easy was it to interpret the results of the assessment?

Since the group of experts had different perspectives and background experiences in pharmacovigilance activities, it was difficult to use the individual rating for indicator selection. Thus, expert group opinion was the appropriate approach in selecting the indicators. In the initial step, the selected experts were asked to determine each individual indicator against the above mentioned validating criteria in the provisional spreadsheet and were asked to provide free-text suggestions as well as discuss with the researcher on how validity of each indicator item could be improved. Then, a haft-day meeting for expert group discussion was held once on 11 July, 2011 to share their views together before the final draft was generated and processed by the researcher.

In practice, the validating process were done to determine only the relevance and practicable of the candidate indicators and assessment questions. The step for determining interpretability could not be complete because pilot testing could cover only some of the candidate indicators according to time constraint and the lack of collection system for some measurements, especially data that must be accessed from other related divisions within the ThaiFDA such as the SMP drug items in a particular timeframe.

The components of expert panel

The expert panel consisted of 7 experts in related fields and took various roles in pharmacovigilance. The experts from outside the ThaiFDA included two academicians from the faculty of pharmaceutical science belonging to the government academic institutes; one is a hospital pharmacist from a regional pharmacovigilance center located in the hospital; and one another from the National Health Security Organization (NHSO) of Thailand. The experts inside the ThaiFDA consisted of the Head of pharmacovigilance unit, the Director and the former Director of the Technical and Planning Division.

CHAPTER IV
RESULTS OF THE STUDY & DISCUSSION

This chapter comprises the results from the indicator development process related to the three-stage model that was explained in the previous chapter. In order to make better understanding of the results from each stage, discussions are simultaneously presented.

4.1 Results on logic model application and scope identification

The procedures in stage 1 aimed to apply logic model to explain performance of the pharmacovigilance functions of the Thai Health Product Vigilance Center (HPVC) and to identify the indicator dimensions or domains. The logical framework for organizational performance assessment (Lusthaus et al., 2002) was applied to use as the conceptual framework for indicator development in this study (see Figure 2.4 in chapter II).

4.1.1 Applying logic model

As described in the chapter II, the organizational assessment model, depicted in Figure 2.4, is a diagnostic tool aimed at helping better understand the performance of an organization, and assess the various components that might affect the performance. The schematic representation of the framework defines performance in terms of effectiveness (mission fulfillment), efficiency, and relevance (the extent to which the organization adapts to changing conditions in its environment). The framework implies that certain contextual forces drive performance: organizational capacity, forces in its external environment, and internal motivation.

Logic model as seen in this logical framework supported the NPVC diagnosis and helped clarify the requirements and resources needed to affect its performance. The advantage of this framework was that it specified organizationally based (the unit of analysis) and focused on a systematic review of the factors that affect organizational performance. Performance in this study was depicted as a set of interactive changes between the organization and its environment in which it

operated. Unlike most assessment models in the past that focused on projects supported by organizations, the logic model using in this study was not project-oriented. While projects are driven by a logic that is relatively linear: inputs lead to activities, which leads to outputs, outcomes, and impacts, respectively, organizational change rarely occurs in this linear pattern (Lusthaus et al., 2002).

Table 4.1 illustrated the selected aspects of each assessment dimension applying in this study.

Table 4.1 Reasons for choosing the framework components for this study

Organizational assessment framework	**Definition**	**Y**	**N**	**Reasons for selection or not to use in this study**
1.Organizational performance	Results of an organization's work on how well or badly the organization does for a particular job or activity			
1.1 Effectiveness	The ability of an organization to successfully meet its objectives or purpose	√		This aspect is a standard parameter for every types of the organization.
1.2 Efficiency	The ability of an organization to maximize the use of its resources to reach its purpose	√		This aspect is also a standard parameter for every types of the organization.
1.3 Relevance	The ability of an organization to satisfy stakeholder requirements, or to respond to external forces		√	This aspect was integrated into some parts of 'Effectiveness'.
1.4 Financial viability	The ability of an organization to generate and manage adequately its resources in order to ensure its ongoing existence		√	The HPVC is a government agency that received annual budget from the government. Thus, financial aspect would not be developed as an indicator.
2.Organizational capacity	The ability of an organization to use its resources to perform its work			

Organizational assessment framework	Definition	Y	N	Reasons for selection or not to use in this study
2.1 Strategic planning / leadership	Strategic planning refers to the pattern of calculated responses to the environment, including resource deployment, that enable an organization to achieve its goals. Leadership is basically the process through which leaders influence the attitudes, behaviors and values of others towards organizational goals.	√	 √	Strategic planning is necessary for the HPVC so as to lead or direct it to accomplish its goals and to guide its operation in the long run. This aspect would not be developed as an indicator, but it would be assessed simultaneously with 'Strategic planning'.
2.2 Structure	The ability of an organization to divide labor and assign roles and responsibilities to individuals and groups in the organization, as well as the process by which the organization attempts to coordinate its labor and groups.	√		Well-organized structure of the HPVC is necessary for both day-to day operation and strategic management.
2.3 Human resources	Human resources planning involves forecasting the human resources needs of the organization, and planning the steps necessary to meet these needs. Staffing an organization means searching for, selecting and orienting individuals who have the appropriate range of knowledge, skills, behavior and values to meet the organization's needs. Developing human resources in an organization means improving employee performance by increasing or improving their skills, knowledge and attitudes.	 √	√ √	This study focused on human resource development, work process and workload of staff in the HPVC. Human resources planning and staffing would not be developed as an indicator, but would be assessed with human resource development.

Organizational assessment framework	Definition	Y	N	Reasons for selection or not to use in this study
2.4 Financial management	Planning, implementing, and monitoring the monetary resources	√		This study explored the annual budgetary allocation to the HPVC.
2.5 Infrastructure	The basic conditions (facilities, technology) that allow an organizational work to proceed	√		Various infrastructures are necessary for the HPVC to operate its work, especially for drug safety surveillance.
2.6 Program management	The ability of an organization to carry out its institutional role	√		Program management referred to the PV program for which the HPVC is responsible. This study explored the PV network either within the country or upon the international level.
2.7 Process management	The ability of an organization to manage the organizational work	√		Process management in this study referred to work process within the HPVC.
2.8 Inter-organizational linkages	The ability of an organization to manage its external relationships		√	This study did not focus on management of stakeholders.
3.Organizational motivation	The driving forces behind the organizational personality			
3.1 History	The story of an organization's inception, growth, awards, achievements, and notable changes in structure or leadership, as well as its failures and near misses		√	This aspect would be integrated to assess the HPVC's mission as a factor that could affect the policies, legal provisions and mission of the HPVC, but it would not be developed as an indicator.
3.2 Mission and vision	An expression of how people see the organization operating	√		Mission statement is necessary to lead and motivate the HPVC to accomplish its goals. This study would include related laws and organizational policies that could affect its mission.

Organizational assessment framework	Definition	Y	N	Reasons for selection or not to use in this study
3.3 Culture	Set of values, guiding beliefs, understandings and ways of thinking that are shared by members of an organization and are taught to new members. Culture represents the unwritten, informal standards of an organization.		√	This aspect would not be developed as an indicator, but it would be integrated into working culture that could drive the HPVC's management.
3.4 Incentives / Rewards	The reason for staff to join an organization, and the way an organization rewards and punishes its staff		√	In general, this aspect did not reflect much in the government agencies and would be integrated as human resource management.
4.Environment	The external factors that affect the organization to survive and perform			
4.1 Administrative / Legal	The formal rules within which the organization operated / the ability of an organization to develop and enforce laws and policies		√	Law, regulations and government administration would not be developed as an indicator, but it would be asked for more details and better understanding such as the incentive policy of the NHSO that could affect ADR monitoring system.
4.2 Political	The ability of an organization to organize civil society among other groups		√	This aspect would not be developed as an indicator, but would be asked for more details and better understanding.
4.3 Social / Cultural	The ability of an organization to shift social and cultural attitudes		√	This aspect would not be developed as an indicator, but would be asked for more details and better understanding.
4.4 Economic	The ability of an organization to develop competition policy framework and manage in the situation of resources constraint		√	This aspect would not be developed as an indicator, but would be asked for more details and better understanding.

Organizational assessment framework	Definition	Y	N	Reasons for selection or not to use in this study
4.5 Stakeholder	The ability of any group within or outside an organization that has a stake or influence in the organization's performance.	√		This aspect is increasingly important. Stakeholders, for example; health institutes within the ADR monitoring network, the WHO-UMC, were included in this study.

From table 4.1, details of each assessment dimension were briefly described as the followings:

Organizational performance

From the logical framework, performance of the NPVC was defined as results of its work on how well or badly the organization did for pharmacovigilance activities. Two dimensions ***Effectiveness*** and ***Efficiency*** were included to use as the main aspects for determining the organizational performance. In general, most of the governmental agencies used 'effectiveness' concept to assess their performance, but few used 'efficiency'. This may be because in assessing efficiency, it is generally more difficult to assess outputs than inputs, especially in governmental organizations, where outputs tend to be qualitative rather than quantitative. This can be seen in some government ministries such as how to assess the efficiency of foreign ministries, whether it is the cost of the ministry in relation to the quality of its international relationships, how is the country image, etc (Lusthaus et al., 2002). Since 'efficiency' is the important concept in the present world to determine whether or not the organization can survive, this study thus employed both effectiveness and efficiency. 'Relevance' and 'Financial viability' did not include in this study.

Effectiveness was defined as (1) the ability of the organization to successfully meet its objectives or purposes or (2) an expression of the degree to which activities have produced the effects as planned. ***Efficiency*** was the ability of the organization to

(1) produce outputs by its minimum resources or (2) the relationship between the results of activities and the corresponding effort expended in terms of money, resources, and time. 'Efficiency' also included the concept of '*administrative efficiency*' that is a measure of how well an organization is managing its strategy and work process.

Organizational capacity

Organizational capacity is the ability of an organization to use its resources to perform. This study examined the capacity of the NPVC in these dimensions: ***structure, human and financial resources, infrastructure, program and process management, and strategic management.*** Within the conceptual framework, this study examined the systems and management practices associated with *human, financial and infrastructure* resources. The examination also included *strategic planning* that referred to the pattern of responses to the environment, including resource deployment, that enable the organization to achieve its goals. *Program management* looked at the ability of the NPVC to carry out PV activities and manage ADR monitoring system, while *process management* examined the way the NPVC manages the main work process within the organization. Finally, *Structure* identified the links between how the organization was governed, and its mission, as well as the roles that human resources and finance play in the organization's daily activities.

Organizational motivation

Organizational motivation represents the underlying personality of the organization in order to understand the driving forces behind it. It is what drives the members of the organization to perform. Within the conceptual framework, this study explored the organization's ***mission*** that include the evolution of mission statement, goals, and role of mission in relation to its purpose and direction. This study included policies and legal framework that referred to the ability of the organization to develop and enforce laws and policies.

External environment

Since organizations are viewed as open systems, support from their environment is needed to survive and perform well. This study examined one dimension of the external environment: ***stakeholder*** that could affect the performance. In assessing the NPVC, stakeholder referred to the ability of the organization to

manage its relationships with health institutes collaborating in ADR monitoring network, as well as institutes outside the organization such as academic institutes, the NHSO, the WHO-UMC, etc.

From the logical framework for organizational assessment and pharmacovigilance activities at the national center, it could be summarized and depicted the concept for indicator development in the following figures:

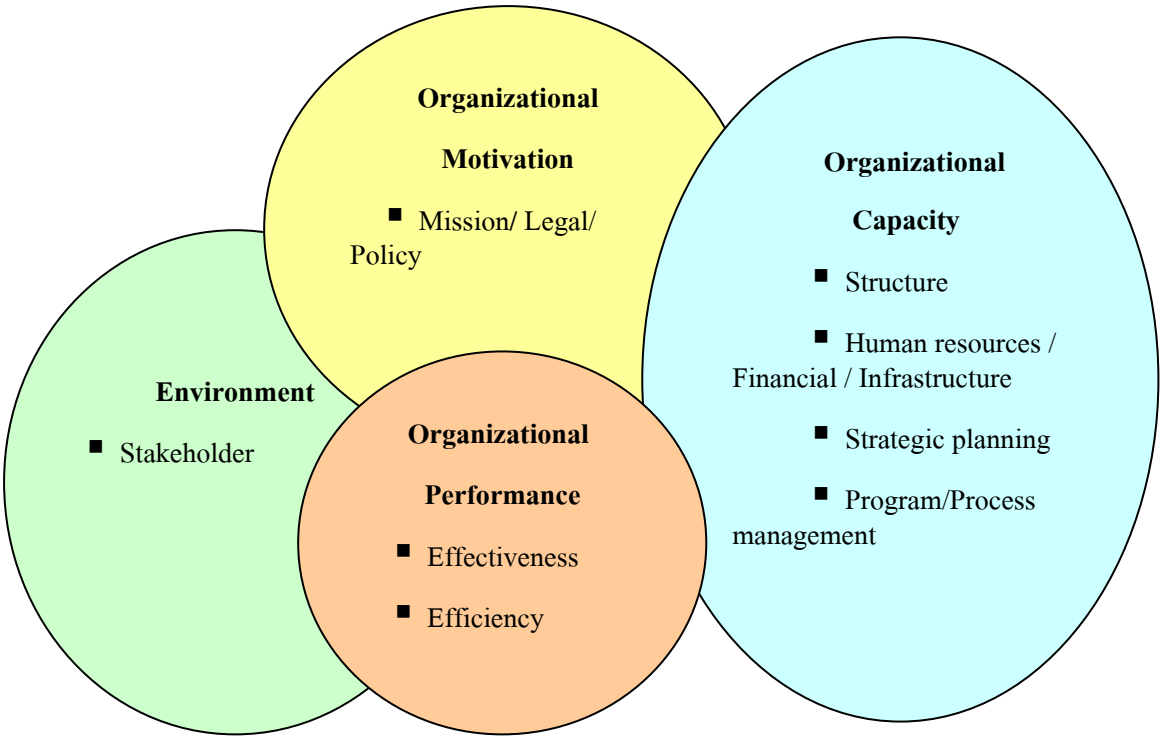

Figure 4.1: Conceptual framework for indicator development

Figure 4.1 illustrated the modified framework for organizational performance assessment using as the conceptual framework in this study.

4.1.2 Identifying scope of the indicators and indicator domains

Regarding the broad definition of pharmacovigilance that includes surveillance activities of any drug-related problems, this study scoped mainly in ADR monitoring system. The pharmacovigilance system in Thailand is managed by the Health Product Vigilance Center (HPVC) as the National Pharmacovigilance Center (NPVC) of the country. The overall purpose of the Health Product Vigilance Center (HPVC) is the reduction of risk to patients and consumers and the improvement of the safety and effectiveness of health products. The missions of the HPVC are as the followings:

- To monitor the safety of all health products under the responsibilities of ThaiFDA (***detection***)
- To detect adverse reactions and new risks as early as possible, with special attention to rare and/or serious adverse effects (***detection***)
- To identify factors associated with adverse effects, such as genetics, gender, age, drug interaction, prescription error, etc., and to establish causality as accurately as possible (***assessment***)
- To reduce risk and prevent or minimise adverse effects across all health products through effective action and communication (***prevention***)
- To encourage all healthcare and other professionals, patients and the public to be aware of ADRs and to use health products, especially medicines, carefully and rationally (***prevention***)

It could be noticed that the missions cover the three essential goals of pharmacovigilance activities defined by WHO, which are ***detection***, ***assessment***, and ***prevention*** of risks to promote the safe use of medicines (WHO, 2002).

The goals in respect of effectiveness and efficiency of the NPVC were defined based on the literature and the official declaration for the organizational establishment. The interviews with the chief of the unit and some executive staffs of the ThaiFDA were done, intended to provide any supplement of the list of goals. However, the interviews showed nearly no new aspects. Most of the interviewees found that in general the scope of pharmacovigilance at the NPVC sufficient and

related to WHO definition. Thus, there was no need to elaborate more on the aspect of additional goals for pharmacovigilance in this study.

The HPVC is responsible for monitoring the safety of health products in Thailand, primarily medicines, including herbal and traditional medicines, through the collection of adverse drug reaction (ADR) reports and the conducting of research. Adverse reaction reports are collected nationwide directly from health facilities or channelled through a national network of regional centers located in 18 tertiary hospitals in rural areas. The HPVC provides the ThaiFDA with information about problems with health products in order for the national authority to take appropriate risk management action by various methods. Safety issues are disseminated throughout the country on a routine basis, and as urgent news when necessary.

Pharmacovigilance activities within the HPVC comprises 4 main elements: 1) Data management of individual case reports of ADRs; 2) Signal detection, risk identification, and risk assessment; 3) Decision making procedure to consider risk minimization tools; and 4) Risk communication, and dissemination of risk minimization tools. These elements were then integrated into the framework for organizational assessment.

Figure 4.2 below showed the indicator domains that were formulated from the combination of the derived conceptual framework for organizational assessment and the main elements of PV functions at the national center. The indicators were distinguished into four domains as the followings: 1) Policy, law, plan, and structural support; this domain explored the enabling factors and struggles that may affect the organizational performance. 2) Safety surveillance; this domain focused on the ADR reporting system in the country, as well as data acquired from various sources. 3) Signal detection and decision making for risk management; this domain included the main work process within the NPVC described in chapter II. And 4) Communication of safety information; this domain explored the communication function of the NPVC.

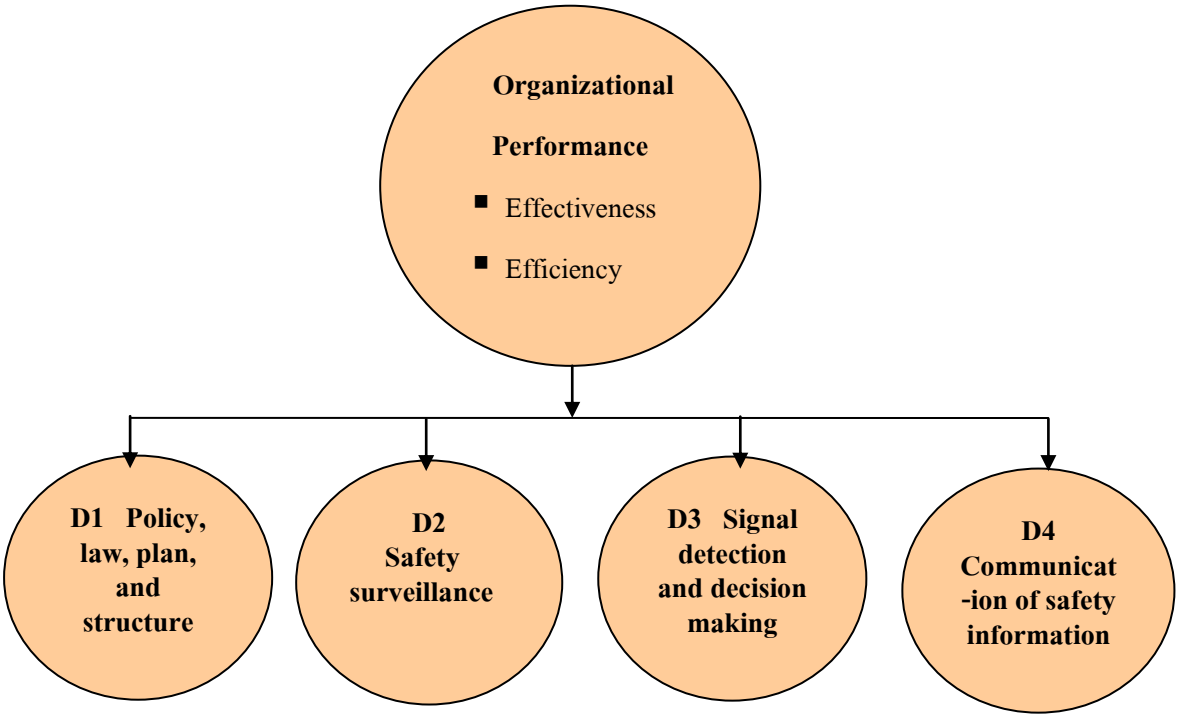

Figure 4.2: Indicator domains linkage to organizational performance

Table 4.2 below showed the linkage between the derived domains of developed indicators (figure 4.2) and the domains in the conceptual framework (figure 4.1).

Table 4.2: Linkage between the derived domains of developed indicators and the domains in the conceptual framework.

Indicator domains (figure 4.2)	**Operational definition**	**Conceptual framework (figure 4.1)**
1.Policy, law, plan and structural support	This domain included policies and legal provisions related to PV that guided the direction, scope, and activities of the NPVC, and PV related strategic plan that guided to achieve goals in the short or longer periods. In this study, they were the NDP and the Drug Act that should incorporate to the mission of the organization. Mission referred to mandate, roles, and responsibilities to handle PV activities. The domain also included the formal structure that was declared officially in the document for organizational establishment, human resources that included both staff within the NPVC; pharmacist and administrative staff, and external experts who provided technical advices on medicine safety issues. The staff (contracted out) working for data verification were also explored. The domain also identified the budgetary allocations that have been provided annually to the NPVC, and tools or equipments that facilitated PV activities such as IT for PV data processing, automatic tool for signal detection.	Organizational motivation (mission/ legal/ policy) Organizational capacity (strategic planning/ structure/ human, financial resources, and infrastructure)

Indicator domains (figure 4.2)	**Operational definition**	**Conceptual framework (figure 4.1)**
2.Safety surveillance	The domain explored the ability to deal with the external relationships of PV activities. It included the system to facilitate safety surveillance such as the national guidelines, SOPs, a standard reporting form, IT for processing PV data. Etc. Program in this study referred to PV program managed by the national center. The main element in this domain was ADR monitoring system in the country. It included the operational plan that guided the NPVC's commitments to achieve program goals, the existence of health institutes contributing in PV activities, the compliance of health institutes on ADR report submission, and ADR reporting rate, as well as ratio of specific types of ADR report.	Organizational capacity (infrastructure/ operational plan/ program management) Environment (stakeholder)
3.Signal detection and decision making for risk management	Process management in this study referred to work process within the NPVC. The domain included monitoring safety information from secondary sources, quality of data acquired (in-house database), the capability for processing data acquired, the reviews of signal detected, and decision making for risk management through the related committee. This domain also explored the ability to communicate safety information and to share knowledge.	Organizational capacity (process management)

Indicator domains (figure 4.2)	Operational definition	Conceptual framework (figure 4.1)
4.Communication of safety information	The domain explored the ability to deal with the external relationships of PV activities both within the country and international level. It included the system to facilitate safety surveillance such as tools and channels for communication of safety information, the national forum held to coordinate of PV activities across all stakeholders, as well as response to external inquiries.	Organizational capacity (infrastructure) Environment (stakeholder)

4.2 Results on the indicator development

The first and second draft indicators were formulated in stage 2. Development concepts and lists of indicators were mainly modified from the following papers:

4.2.1 Sources of the list of indicators

1) the report of regulatory PV indicators

1.1) the report of Amrumpai et al. (2007). The indicators in this report provided broad-spectrum drug safety–specific indicators identified through the structure, process, and outcome model. The report was the frame for drafting the list of indicators, but did not provide the assessment questions.

1.2) the recommended PV indicators in the report of WHO, conducted by Ratanawijitrasin et al. (2002) (S1). This report enhanced to see more detailed indicators. As mentioned in that report, the voluntary nature of ADR reporting by health professionals means that the number of reports received by an ADR centre depends very much on the awareness and active participation of physicians, pharmacists and other health personnel. Because countries differ in the size of their human resources for health and in the number of drugs available, the performance of an ADR reporting system should be investigated in terms of both those variables.

2) the Fraunhofer report (S2)

Regarding the main work process of the NPVC, the–main elements of PV activities congruence with those identified in this report. However, most of them were used to measure and showed only the data that described the productivity of the work, such as number of ICSRs processed, number of PSURs assessed, number of responses to inquiries, number of market withdrawals of drugs compared to other countries, etc.

Like the situation in Thailand and other countries, the Fraunhofer report mentioned about the difficulties in designs of the measuring PV system, such as the outcomes and impacts could not be adequately measured with the existing data. The number of market withdrawals was difficult to interprete because these result caused from different reasons including internal decisions within the MAHs other than safety concerns. Reporting rates were also difficult to interprete because they were input factors for the system at the national level but partially the output of approaches to improve reporting system. However, the first and second draft indicators in this study (see Appendix B and C) were mainly employed from the list of indicators from the Fraunhofer report.

3) the SPS report for the USAID (S3)

Most of the indicators in this report were structure indicators that provided qualitative data. In the SPS report, the Indicator-Based Pharmacovigilance Assessment Tool (IPAT) was developed as a comprehensive performance metric for pharmacovigilance and medicine safety systems. This study borrowed some indicators, especially regarding the component 1) Policy, law, and regulation, and 2) Systems, structures, and stakeholder coordination. These components derived from the SPS report and make adaptation for the appropriateness.

4.2.2 Indicator formulation

1) All identified candidate indicators

After all the identified candidate indicators from literature review were listed, they were adjusted and adopted to the organizational context. Then, some identical, repeated, or similar indicators were removed. After that, assessment questions based on the candidate indicators were generated. Finally, a second draft of candidate

indicators were formulated (see Appendix C). The second draft indicators were distinguished into 6 domains as follow: 1) Policy and plan, 2) Acquiring data input, 3) Data processing, 4) Data analysis, 5) Decision making for risk minimization strategies, 6) Communication of safety information.

2) Validated indicators

In stage 3, indicator validation through expert opinions against predefined criteria was conducted. The expert panel meeting was held for discussion based on 'relevance' and 'practicability' criteria. For 'interpretability' criteria, some candidate indicators were collected data to serve for pilot testing. The indicators were then refined and categorized. The final draft of validated indicators was finally summarized and generated by the researcher.

Table 4.3 below showed domains of the list of indicators both the full lists that borrowed from various sources and the selected lists. The table also displayed sources of the full-listed indicators, as well as opinions and recommendations for each indicator.

S1 = the WHO report by Ratanawijitrasin et al. (2002),

S2 = the Fraunhofer report,

S3 = the SPS report for USAID,

S4 = initiated by the researcher,

S5 = other sources; specified.

R = Relevance, and P = Practicability were criteria for validating the indicators.

Table 4.3(1): Policy, law, plans, and structural support

The selected indicators (final lists)	The candidate indicators (full lists)	S	R	P	Recommenda-tions
Subdomain1: policy, law, and plans					
1.1 Existence of a policy related to PV (structure indicator)	1) Existence of a policy document that contains essential statements on PV	S3	√	√	
	2) Number of documents prepared (legal acts, guidelines)	S2	√	√	Denominators should be identified.
1.2 Existence of legal provisions for PV (structure indicator)	1) Existence of specific legal provisions for PV	S3	√	√	
1.3 Existence of strategic plans or annual operational plans (structure indicator)		S4	√	√	This indicator was initiated by the researcher./ Strategic and operational plans may be stated in organizational structure.

The indicators in this domain were quantitative (yes/ no) questions. Subsequent qualitative questions should be asked to be able to explain more about the results from the assessment. The relevance of plans, related laws, and policies could be used as the criteria for determining the results. Law in this study focused on the Drug Act, and policy focused on the National Drug Policy. Any other laws and policies may be specifically focused, based on objectives of the studies. Strategic and operational plans may be stated in the organizational structure, but in this study they were grouped into law and policy domain.

Table 4.3(1): Policy, law, plans, and structural support (cont.)

The selected indicators (final lists)	The candidate indicators (full lists)	S	R	P	Recommenda-tions
Subdomain 2: structural support					
1.4 Presence of good oganizational management (structure indicator)	1) Existence of PV center 2) PV unit has a clear mandate, structure, roles and responsibilities	S3 S3	√ √	√ √	Subsequent qualitative questions should be asked.
1.5 Human resource management (structure indicator)	1) A designated staff responsible for PV 2) Availability of external expertise for routine cases 3) Number of staff in full-time equivalents 4) Total number of staff including regional centers for routine work 5) % of staff trained per year	S3 S2 S2 S2 S2	√ √ √ √ √	√ √ √ √ √	The denominators should be defined for some indicators (no.4,5) such as number of staff per total number of pharmacists in the whole country.
1.6 Dedicated budget available for PV-related activities (structure indicator)	1) Dedicated budget available for PV activities 10) Annual budget of the agency	S3 S2	√ √	√ √	Data should be collected for several years to see time-trend.
1.7 Existence of a system to facilitate drug safety surveillance (structure indicator)	1) Guidelines and a procedure 2) Routine training/ information 3) System for providing feedback 4) Existence of PV guidelines, SOPs, ADR reporting form	S5 S5 S5 S3	√ √ √ √	√ √ √ √	WHO, AEFI WHO, AEFI WHO, AEFI
1.8 Existence of PV national forum (structure indicator)	1) Platform exists for the coordination of PV	S3	√	√	
1.9 Existence of a national medicine safety advisory committee or a subcommittee with similar functions (structure indicator)	7) Existence of a national medicine safety advisory committee or a subcommittee	S3	√	√	Subsequent qualitative questions should be asked.

This domain contained quantitative (yes/ no) questions, thus subsequent qualitative questions should be asked. Some indicators should be defined the denominators in order to make them more meaningful and comparable.

Table 4.3(2): Safety surveillance

The selected indicators (final lists)	The candidate indicators (full lists)	S	R	P	Recommenda-tions
Subdomain1: safety surveillance within the country					
2.1 Percentage of health institutes contributing in PV activities (structure indicator)	1) Existence of a system for coordination and collation of PV data from all sources in the country (yes/ no question)	S3	√	√	Subsequent qualitative questions should be asked.
2.2 ADR reporting rate (outcome indicator)	1) The ratio of the average number of ADR reports to the number of physicians and pharmacists	S1	√	√	In Thailand, pharmacists played the major role in PV activities.
	2) The ratio of the average number of ADR reports to the number of drugs registered in each of the countries	S1	√	×	Data on drug registered in a particular period
	3) Number of ADR report received in the last year	S3	√	√	were not easy to access.
	4) Total number of ICSRs	S2	√	√	The denominators
	5) Number of ICSRs from MAHs, HCPs, pharmacists, other HCPs	S2	√	√	for indicators no.3,4,5 should be defined.
	6)Number of cases received/ total number of ICSRs	S2	√	×	Number of real cases (incidence)
	7) Total reporting rate per million inhabitants	S2	√	√	were not easy to access.
	8) Reporting rate in children per million inhabitants	S2	√	√	

Although health institutes are the major mechnisms for collaborating PV activities in every countries, few studies used health institutes directly as an indicator.

Reporting rate per number of population would be developed to be an indicator in this study. It could be sub-analyzed in any groups such as the elderly, the children. In Thailand, only pharmacists played the major role in PV activities, thus, number of population, instead of number of healthcare providers, were determined to use as the denominator.

Table 4.3(2): Safety surveillance (cont.)

The selected indicators (final lists)	**The candidate indicators (full lists)**	**S**	**R**	**P**	**Recommenda-tions**
2.3 Ratio of specific types of ADR report and total reports (outcome indicator)	1) Percentage of patients with serious, unexpected adverse events 2) % of serious ICSRs	S3 S2	√ √	√ √	Denominators should be defined clearly.
2.4 Compliance with time requirement for ADR report submission (process indicator)	1) Compliance of report providers with dates or legal requirements	S2	√	√	

Table 4.3(2): Safety surveillance (cont.)

The selected indicators (final lists)	**The candidate indicators (full lists)**	**S**	**R**	**P**	**Recommenda-tions**
Subdomain 2: Safety surveillance from secondary sources					
2.5 Monitoring of drug safety information from secondary sources (process indicator)	1) Number of medicine safety issues of local relevance identified from outside sources (e.g., from another country, or from regional or international sources) 2) Use of information from other agencies 3) Access to all necessary data	S3 S2 S2	√ √ √	√ √ ×	 It was impossible to access to all necessary data, even though it should be.

Table 4.3(3): Signal detection and decision making for risk management

The selected indicators (final lists)	The candidate indicators (full lists)	S	R	P	Recommenda-tions
3.1 Capability to prepare data ready to be analyzed (process indicator)	1) Number of ICSRs processed	S2	√	√	Denominators should be defined.
3.2 Quality of data acquired (in-house database) (outcome indicator)		S5	√	×	This indicator derived from WHO-UMC.
3.3 Automated signal detection (process indicator)	1) Information for signal detection, data sources, available statistical tools	S2	√	√	
	2) Time between detection of signal and publishing	S2	√	√	
3.4 Decision making for risk management (process indicator)	1)Average time lag between identification of safety signal and communication	S3	√	√	
	2) Come to decisions in good time	S2	√	×	'Good time' should be defined clearly.
	3) Time from first signal to action	S2	√	×	
	4) Implement decisions in good time	S2	√	×	
	5) Number of drug withdrawals, suspensions, changes in SPCs	S2	√	√	Denominators should be defined.

The assessment questions for data quality in this study were derived from the WHO-UMC. However, according to the complex structure of PV data, it was difficult to implement the indicator no.3.2. The HPVC should start preparing the supportive database and system for utilization this indicator.

Table 4.3(4): Communication of safety information

The selected indicators (final lists)	The candidate indicators (full lists)	S	R	P	Recommenda-tions
4.1 Effectiveness of safety information communication (outcome indicator)	1) Existence of medicine safety bulletins	S3	√	√	
	2) Number of "Dear health care professional" letters or other safety alerts developed and distributed	S3	√	√	
	3) Reaching targets for timing of communication	S2	√	×	It was not practicable to routinely assess stakeholders.
	4) Consistency of communication across stakeholders	S2	√	×	
	5) Number of dear doctor letters sent	S2	√	√	
4.2 Knowledge sharing (outcome indicator)	1) Number of public education activities	S3	√	√	Denominators should be defined.
	2) Number of scientific publications with at least one author from the agency	S2	√	√	
4.3Response to external inquiries (outcome indicator)	1) Number of drug safety information requests received and addressed	S3	√	√	Denominators should be defined.
	2) Number of responses to inquiries	S2	√	√	
	3) Number of other answered queries	S2	√	√	

Most of the developed indicators in this domain were yes/no questions, thus subsequent qualitative questions should be asked for better understanding the results from the assessment.

4.3 Final revision of the validated indicators

Indicator validation through expert opinions was conducted in stage 3. The expert panel meeting for discussion about the relevance and practicability of the candidate indicators was held once, half-day in july, 2011. The indicators were then refined and categorized regarding the recommendation from the meeting and congruence with the conceptual framework set in stage 1. Finally, the final draft indicators were generated. They were distinguished into 4 domains as follow: 1) Policy, law, plan, and structural support, 2) Safety surveillance, 3) Signal detection and decision making for risk management, and 4) Communication of safety information.

Domain 1: Policy, Law, Plan and Structural support

The indicators in this domain will be used to identify the existence of and the relevance of legal provisions, policy, and plans in each level, and also examine the organizational structure which included guidelines, SOPs, protocols, dedicated budget, designated staff, facility infrastructure, and related committees. They reflected the enabling factors to enhance the successful towards the organizational goals. Thus all of them will be used to assess the effectiveness of the NPVC. This domain contained 2 subdomains: 1) policy, law, and plans, by which the organization uses to lead its operations, and 2) organizational structure that included personnel, budget, facility infrastructure such as IT, guidelines, and so on.

Subdomain 1; Policy, law, and plan comprised 3 indicators:

1.1) A policy statement related to pharmacovigilance (PV)

1.2) Existence of legal provisions for PV

1.3) Existence of strategic plan or annual operational plan

Subdomain 2; Organizational structural support comprised 6 indicators:

1.4) Presence of good oganizational management

1.5) Human resource management

1.6) Dedicated budget available for PV-related activities

1.7) Existence of a system to facilitate drug safety surveillance

1.8) Existence of PV national forums

1.9) Existence of an ADR or drug safety advisory committee or a subcommittee with a functional activity related to PV

Domain 2: Safety surveillance

One of the major roles of the NPVC is to monitor safety information of both those occurred in the boundary of Thailand and in the global level. The indicators in this domain reflect the capability of the organization to participate and build partnerships, and bring multiple stakeholders together for successful information exchange. It refers to the coordination and collation of data between data providers and the national center (NPVC), timely and effective data flow, as well as the quality of data obtained from secondary sources. This domain contains 2 subdomains: 1) the function of the NPVC to provide safety surveillance in the country, and 2) the function to monitor safety information from the secondary sources such as Drug Regulatory Authority (DRA) in other countries, corresponding news, e.g. BBC, CNN, etc.

Subdomain 1; Safety surveillance within the country comprised 4 core indicators:

2.1) Percentage of health institutes contributing in PV activity

2.2) ADR reporting rate

2.3) Ratio of specific types of ADR report and total reports

2.4) Compliance with time requirement for ADR report submission

Subdomain 2; Safety surveillance from seconadary sources comprised 1 core indicator:

2.5) Monitoring of drug safety information from secondary sources

Domain 3: Signal detection and decision making for risk management

This domain refers to the function of the NPVC to collect, summarize, and transform of ADR information; to identify, estimate, and evaluate the volume and seriousness of risks that associated with a pharmaceutical product; and to propose the corrective measures to minimize risks. 4 main indicators, as the followings; capability to prepare data ready to be analyzed; quality of data acquired (in-house database); automated signal detection; and decision making for risk management, were developed. They reflect the capability of the organization to manage large dataset in order to generate drug safety signal and make decisions for risk management. 4 core indicators were as the followings:

3.1) Capability to prepare data ready to be analyzed

3.2) Quality of data acquired (in-house database)

3.3) Automated signal detection

3.4) Decision making for risk management

Domain 4: Communication of safety information

The indicators in this domain reflect the capability of the organization to organize timely and effective dissemination of safety information, and its responsiveness to any related queries either in domestic level or international level in order to facilitate safety surveillance. 3 core indicators were developed as the followings:

4.1) Effectiveness of safety information communication

4.2) Knowledge sharing

4.3) Response to external inquiries

Summary of the validated indicators, including all assessment questions, was displayed in **Table 4.4**, and the detailed descriptions of each indicator were described in **Appendix A**. In table 4.4, **data source** revealed the location of the data to be used in calculating the measure, including databases, tracking tools, or specific roles within the NPVC that can provide required information. **Standard criteria** referred to criteria or cut point for conclusions.

Table 4.4: Summary of the validated indicators (Final draft)

Domain 1: Policy, Law, Plan and Structural support:

The indicators in this domain could be used to identify the existence of and the relevance of legal provisions, policy, and plans in various levels, and also to examine the organizational structure which includes guidelines, SOPs, protocols, dedicated budget, designated staff, facility infrastructure, and related committees. They reflect the enabling factors to enhance the successful towards the organizational goals. This domain contains 2 subdomains: 1) policy, law, and plans, by which the organization uses to lead its operations, and 2) organizational structure that includes personnel, budget, facility infrastructure such as IT, guidelines, and so on.

Indicator number	Indicator	Assessment questions / measurements	Data sources	Standard criteria
	Policy, law and plans			
1.1	A policy statement related to pharmacovigilance (PV)	1.Is there a statement of national policy specified on PV? (Y/N) What are they? Please specify. 2.Is there a standard procedure for reviewing a policy? (supplementary) 3.Has the policy been reviewed periodically? (supplementary)	NDP, National PV policy, MoPH policy documents, and other related policy documents	Advocacy for PV activities should be provided and available within the national policy documents.
1.2	Existence of legal provisions for PV	1. Are there legal provisions related to PV? What are they? Please specify. 2. What is the specific act or regulation of the legislation that serves for PV? 3. Does the law connect to the policy previously identified? 4. Has the law been reviewed periodically? How often has it been reviewed? (supplementary)	The Drug Act, pharmaceutical legislation and regulations, other related laws and policy documents	Legislation for PV activities should be provided in the country.
1.3	Existence of strategic plans or annual operational plans	1. Is there a strategic plan or annual operational plan for PV activities? Please describe what they are. 2. Are these plans tied up with the policy or laws stated previously?	Organizational strategic plan, annual operational plan, and evaluation report	The document of a strategic plan, and an annual operational plan should be available.

		3. Have the strategic plan and operational plans been reviewed periodically? 4. How have they implemented?	documents	Such a plan should have been implemented.
	Structural support			
1.4	Presence of good oganizational management	1. Is there a clear organizational mandate? 2. Is there organizational structure? 3. Is there designated role and responsibility for specific task?	The Drug Act and related laws, the declaration document for establishment of the national PV center	The formal detailed documents for establishment of the national PV center should be available and have been operationalized and implemented. PV center should have a clear mandate, structure, roles, and responsibilities.
1.5	Human resource management	1.Is each staff assigned a specific responsibility? 2.Does the organization evaluate workload and number of staff? 3.Has the national pharmacovigilance center commissioned the advisory committee or subcommittee or ad hoc working groups responsible for providing technical advice on medicine safety issue? How were the members of the committee or the working group recruited?	Documents of job description of the PV center	Job description of specific PV responsibility should be provided, and announced for the designated staff.
1.6	Dedicated budget available for PV-related activities	1. Is there a specific budgetary allocation for annually planned PV activities? 2. Is the budget sufficient for each of the planned activities?	Budget allocation documents	The government should provide annually appropriated funding for the center to support

				its activities.
1.7	Existence of a system to facilitate drug safety surveillance	1.Is there a standard operating procedure/guideline for staff at National PV center to follow? 2.Is there a standard operating procedure/guideline for ADR reporters to follow? 3.Is there standard form for PV data collection? 4.Does the national pharmacovigilance center have (workable) hardware and software to manage data? 5.Is there an IT maintenance system ?	National PV guideline documents, database review, sample of ADR reports received, other related documents.	National PV guidelines should be available and periodically revised. Any forms for ADR or drug safety issue reporting should be developed and routinely used in the locations of data providers. They should be revised to ensure the consistency with international standards and the requirements for data analysis. In addition, ADR or other PV data warehouse that contains data from all sources, as well as IT system should be developed.
1.8	Existence of PV national forums	1.Does the national pharmacovigilance center arrange a platform or forum that all stakeholders may attend? 2.How often have the forums been held? How many people attend the forum? 3 Is there any issue being generated from the forum? Whether there is any action taken for those issues?	Reports of work accomplishment	A formal forum for PV coordination should be conducted at least once a year.
1.9	Existence of an ADR or drug safety advisory	1. Does an ADR or drug safety advisory committee or a subcommittee exist to provide technical advice to the	The Drug Act and related laws and	Such a committee should be advocated for

	committee or a subcommittee with a functional activity related to PV	ThaiFDA on drug safety issues? 2. Does the committee or subcommittee meet regularly or at least once a year?	regulations; minutes of the national drug safety advisory committee meetings	the establishment, and developing terms of reference for its mandate should be supported.

Domain 2: Safety surveillance

One of the major roles of the NPVC is to monitor safety information of both those occurred in the boundary of Thailand and in the global level. The indicators in this domain reflect the capability of the organization to participate and build partnerships, and bring multiple stakeholders together for successful information exchange. It refers to the coordination and collation of data between data providers and the national center (NPVC), timely and effective data flow, as well as the quality of data obtained from secondary sources. This domain contains 2 subdomains: 1) the function of the NPVC to provide safety surveillance in the country, and 2) the function to monitor safety information from the secondary sources such as Drug Regulatory Authority (DRA) in other countries, corresponding news, e.g. BBC, CNN, etc.

Indicator number	**Indicator**	**Assessment questions / measurements**	**Data sources**	**Standard criteria**
	Safety surveillance within the country			
2.1	Percentage of health institutes contributing in PV activity	How many percent of health institutes summitted ADR report? Analysis can be conducted on:- 1)**types of settings**: Percentage of health institutes (reporting sources) with functional PV activity (submitting >= 1 report annually to the NPVC) 2)**geographic areas**: Percentage of health institutes (reporting sources) in	Database review, documents of the MoPH statistics unit (for number of health institutes in the country)	1)100 percent of health institutes are expected to contribute. 2)100 percent are expected to submit reports via electronic submission.

		each region with functional PV activity (submitting >= 1 report annually to the NPVC) 3)**types of settings by channel of report submission**: Percentage of hardcopy reporting sources and those of electronic sources *Note:* (1)functional PV activity means submit >= 1 report in a given year. (2)types of health institutes include:- (2.1) public hospitals (2.2) private hospitals (2.3) health centres and other institutes (2.4) community pharmacy / drug store (2.5) MAH / registered pharmaceutical manufacturing industry (voluntary reporting) (3)geographic areas include:- BKK, the vicinity of BKK, northern, southern, northeastern, western, eastern, and central part of Thailand		
2.2	ADR reporting rate	1) Number of reports received in a given year per number of million population for the whole country; midyear population *Note*: Analysis can be conducted as a supplementary measurement on:- Number of reports received in a given year per million inhabitants in each region (BKK/ vicinity of BKK/ north/ south/ north-east/ west/ east/ central part of Thailand)	Database review, documents of the national statistics department of Thailand (for the number of midyear population)	No standard criteria are available.

2.3	Ratio of specific types of ADR report and total reports	1) Number of serious ICSRs (Individual Case Safety Reports) per total number of reports received in a given year 2) Number of suspected new drug-ADR reports per total number of reports received in a given year *Note*: new drug means drug registered not more than 5 years. 3) Number of reported drug items in SMP per total number of SMP drug items in a given year	Database review	1)No standard criteria are available for reporting rate of serious ICSRs or ADRs related to new drugs. 2)All of SMP drug items are expected to be reported.
2.4	Compliance with time requirement for ADR report submission	How many of ADR reports submitted within time requirement? 1)Percentage of ADR report with death case submitted within time requirement (48 hrs after detected) 2)How frequently ADR reports submitted annually? *Note*: (1)For hard copies, considered time means time during date of ADR detection and report arrival date at the NPVC (2)Analysis can be conducted on:- (2.1) hard copies (2.2) electronic submission	Database review	1)100 percent of ADR reports with death case are expected to be submitted within time requirement. 2)All of ADR reports are expected to be submitted to the NPVC not less than 6 times a year.
	Safety surveillance from secondary sources (e.g. DRA website, corresponding news)			
2.5	Monitoring of drug safety information from secondary	1)How frequently the assigned staff monitor safety information from specified secondary sources? (every day/ every 2 days/ every week/ >every week)	Chief and staff of the NPVC , reports of work	The assigned staff is expected to monitor safety information from

	sources	2)If the risk or safety information from secondary sources is not clear, did the assigned staff acquire supporting information regarding the magnitude of risk or statistical results or other important information?	accomplishment	secondary sources every day, and also acquire additional important information when the information from specified sources is not clear.

Domain 3: Signal detection and decision making for risk management

This domain refers to the function of the NC to collect, summarize, and transform of ADR information; to identify, estimate, and evaluate the volume and seriousness of risks that associated with a pharmaceutical product; and to propose the corrective measures to minimize risks. 4 main indicators, as the followings; capability to prepare data ready to be analyzed; quality of data acquired (in-house database); automated signal detection; and decision making for risk management, were developed. They reflect the capability of the organization to manage large dataset in order to generate drug safety signal and make decisions for risk management

Indicator number	Indicator	Assessment questions / measurements	Data sources	Standard criteria
3.1	Capability to prepare data ready to be analyzed	1.Percentage of reports in the database that have been verified? 2.How efficiently the responsible staff work on verifying new coming reports?	Database review, Workload review	1)100 percent of reports in the database are expected to be verified 2)There is no standard criteria available to determine workload.
3.2	Quality of data acquired (in-house database) (The measurements were derived from WHO-UMC)	1.**Report completeness**-Percentage of key data fields that were filled in (quantitative measurement): This indicator was designed as a sum of scores for defined key data fields to measure the overall completeness of each report, e.g. 70 percent of the key fields were filled in.	Database review	No standard criteria are available now.

		2.**Missing data**-Key data items that were often not filled in (qualitative measurement): *Note*: "often" must be clarified. This indicator was designed to check the data items that were often missing. 3.**Data accuracy or incorrect translation**-Percentage of data fields that the reported values matched predefined values in translated terminologies or look-up tables: This indicator was designed to check of filled-in values in each data field against predefined values in the corresponding controlled or translated terminologies. 4.**Data consistency**-Percentage of logically linked fields that the reported information were in conflict: This indicator was designed to check of a field-field comparison with predefined logical checks. Examples of consistency checks were as the followings; date of onset must not be before start of treatment with suspected drug; pregnancy must be women only.		
3.3	Automated signal detection	Percentage of potential signals that have been completely reviewed and analyzed	Database review, Minutes of the Signal Review Panel meetings	100 percent of potential signals generated by automated tool are expected to be reviewed and proposed for risk management.
3.4	Decision making for risk management	1. How often does the subcommittee meet? 2. Are there any standard criteria for the subcommittee using in making the decision? 3. Lead time spending on decision making through the	Minutes of the national drug safety advisory subcommittee	Criteria for the subcommittee using as the principle in decision making should be

		advisory subcommittee	meetings	developed. For lead time spending on making decision, there have been no standard criteria available.

Domain 4: Communication of safety information

The indicators in this domain reflects the capability of the organization to organize timely and effective dissemination of safety information, and its responsiveness to any related queries either in domestic level or international level in order to facilitate safety surveillance. 3 core indicators have been developed as the followings:-

Indicator number	Indicator	Assessment questions / measurements	Data sources	Standard criteria
4.1	Effectiveness of safety information communication	1.Does the NPVC communicate safety information to its targeted audiences? Please specify who is the targeted audiences. (e.g.health professionals / the MAHs / general public, etc.) 2.Does the NPVC utilize a variety of channel for communication? Please specify. What is the most functioning channel? 3.How fast the information has been distributed? *Note*: Analysis can be conducted on serious or non-serious information.	Documents of the NPVC such as plans, SOPs	No standard criteria are available for speed of communication. However, the information are expected to be disseminted to all targeted audiences.

4.2	Knowledge sharing	1. Is there a publication authored by at least one of the NPVC staff existing in the PV related journals? How many of the publications in a year? Please specify the topics which have been published. 2. Has public education conference or academic seminar been held to transfer knowledge from the NPVC to other institutes? If so, how often the conference or seminar has been held? Who attended? Please specify the topics discussed.	Publication review on the national and international related journals, other related documents	No standard criteria are available.
4.3	Response to external inquiries	1. Is there the query-response service existing in the NPVC? If so, how many of communication channels providing the activity? Please specify. 2. Is there an assigned staff responsible for this job? 3. Percentage of questions or inquiries that have been answered or fed back 4. What is the average responding time? Note: Analysis can be conducted regarding groups of people to be responded.	Database review, reports of work accomplishment	100 percent of the queries are expected to be responded. However, no standard criteria are available for responding time.

CHAPTER V
CONCLUSION & RECOMMENDATION

This chapter contained a conclusion on major findings of the indicators that were developed. Recommendations and suggestions were finally stated.

5.1 Conclusion

The goal of this study was to develop a set of indicators to assess the performance of the national center for pharmacovigilance in Thailand. The study was initiated in response to the recognition of the need to systematically evaluate phamacovigilance system, but the lack of comprehensive tools. The indicators were designed for assessing the organizational performance in two aspects; effectiveness and efficiency. The methodology of this study comprised 3 stages: 1) applying logic model and identifying indicator domains; this stage aimed to identify the main functional PV activities of the HPVC and the factors within the organization, as well as the external environment that could affect its performance. Literature review was the main method in this stage. Observation during work-hour, face-to-face interviews with some administrative staff, and informal discussions with some staff at higher level were also done. 2) formulating the candidate indicator; this stage was the important and longer process, aimed to serve the objective of the study. The first and second draft indicators were initiated in this stage. Literature review provided the main sources of the list of candidate indicators. After listing all the identified and related indicators, they were adjusted and adopted to the organizational context. Some identical, repeated, or similar indicators were removed. Then the assessment questions based on the candidate indicators were generated and listed alongside the indicators. The iterative process for indicator refinement continued until saturated. 3) validating the candidate indicators through expert opinions against predefined criteria, the final stage in this study aimed to ensure the validity and practicability of the developed indicators. The final revision of the indicators was generated by the researcher.

Finally, twenty-one indicators were developed and were judged against the predefined validating criteria. The set of validated indicators consisted of four domains: 1) policy, law, plan, and structural support, 2) safety surveillance, 3) signal detection and decision making for risk management, and 4) communication of safety information. Details of each domain were briefly described as the followings:

Domain 1: policy, law, plan, and structural support, this domain comprised 9 indicators, which could be used to identify the existence of and the relevance of legal provisions, policy, and plans in each level, and also to examine the organizational structure which included guidelines, SOPs, protocols, dedicated budget, designated staff, facility infrastructure, and related committees. They reflected the enabling factors to enhance the successful towards the organizational goals. This domain contained 2 subdomains: 1) policy, law, mission and plans, by which the organization used to lead its operations, and 2) organizational structure that included personnel, budget, facility infrastructure such as IT, guidelines, and so on.

Domain 2: safety surveillance comprised 5 indicators. The indicators in this domain reflected the capability of the organization to participate and build partnerships, and brought multiple stakeholders together for successful information exchange. It referred to the coordination and collation of data between data providers and the national center, timely and effective data flow, as well as the quality of data obtained from secondary sources. This domain contained 2 subdomains: 1) the function of the NPVC to provide safety surveillance in the country, and 2) the function to monitor safety information from the secondary sources such as Drug Regulatory Authority (DRA) in other countries, corresponding news, e.g. BBC, CNN, etc.

Domain 3: signal detection and decision making for risk management, comprised 4 indicators. This domain referred to the function of the NPVC to collect, summarize, and transform of ADR information; to identify, estimate, and evaluate the volume and seriousness of risks that associated with a pharmaceutical product; and to propose the corrective measures to minimize risks. Four main indicators, as the

followings; capability to prepare data ready to be analyzed, quality of data acquired, automated signal detection, and decision making for risk management, were developed. They reflected the capability of the organization to manage large dataset and make decisions for risk management.

Domain 4: communication of safety information comprised 3 indicators. The indicators in this domain reflected the capability of the organization to organize timely and effective dissemination of safety information, and its responsiveness to any related queries either in domestic level or international level in order to facilitate safety surveillance.

5.2 Strength and limitation of the study

The strength of this study was that it used logic model, derived from the work of Lusthaus et al.(2002), for the organizational assessment to be the framework for indicator development. The model was borrowed and applied for an assessment framework that focused on the following areas: 1) measuring organizational performance, 2) understanding the organization's external environment, and 3) determining organizational motivation and examining organizational capacity. The model then detailed out the major issues and dimensions relating to the organizational level. The attributes, selected to identify the NPVC's performance, were be able to clarify the complexity of the organization. For example, mission and strategy could explain the interactive relationship between the NPVC and its clients within the broader PV system. They led the direction of the NPVC and also contributed the PV network in the country. The study also included policy dimension, legal and regulatory dimension, which identify the external context that could promote, facilitate, or obstruct the NPVC's work.

However, one of the limitations of the developed indicators in this study was that most of them derived for qualitative data, thus, experience of the assessor was the most important factor in interpretation of the results. The qualitative indicators needed more details to support a completed assessment, thus the assessor who used them

should find out more information to explain the results. The results from specified qualitative indicators were more subjective and needed more clarified standard criteria to determine them. Further studies might clarify more on the standard criteria for qualitative indicators developed from this study.

It might be argued that the advantage of qualitative indicators was that they were easy for using because the questions were straightforward to the point, while quantitative indicators were more difficult to formulate, but once the data were obtained, it was easier to interpret the numerical results.

Another limitation was that some validated indicators have not been tested according to time constraint. However, the HPVC could use this set of indicators as the initiated tool to improve its performance in the future.

5.3 Recommendations for further actions and future study

The indicator development for performance assessment could suggest that Thailand has a considerably well-established policy, law, and plans related to PV activities. The national PV center has a well-established structure and clear mission to guide its roles and responsibilities. The network for ADR reporting system also well established and effectively operated. Some lags exist in monitoring and evaluating system of the organizational performance. The HPVC has to be responsible for assessing its own functions, thus the systematic evaluation system should be set up and carried out to enable the agency to learn about its performance and identify obstruction and opportunities for improvement.

In addition, from the listing of the various attributes of the organizational performance, it could be noted that the emphasis of this study was on identifying internal capacity (human resources, structural support, and effective resource use) as well as some internal motivation. For better understanding and responding to the importance of the external environment and broader context, further studies should concern more on these attributes such as stakeholder satisfaction, the influence of

various interested groups within the PV network affecting the performance of the NPVC. By analyzing, designing and using more meaningful PV indicators, managers and others can evaluate and communicate how well the organization is responding to major environmental problems. The NPVC should initiate and establish mechanisms to regularly monitor how the many aspects of its performance are being carried out and to evaluate outcomes of PV activities if possible.

Since there are multiple stakeholders and key players within the PV network, it is considerably necessary to use multiple indicators to provide a full understanding of the organizational performance. Because safety information can emerge from ADR reporting system, it is essential to create an effective information management system that can provide timely, accuracy and quality ADR information to be used as input for signal generation and drug safety alert.

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APPENDICES

Appendix A

Final revision of the validated indicators

Presentation Format of the developed indicators (Applied from the SPS report)

Heading	**Description**
Indicator number and name	The number of the indicator and its name
Effectiveness or Efficiency	Aspects of the organizational performance to be assessed
Purpose	A statement of the purpose for using the indicator
Rationale	A statement of why the indicator is important and relevant for assessing the performance
Data collection	Description of the ways data were collected and/or reviewed
Collection frequencies	The frequency of data collection, which was based on a rate of change in particular objects that were being assessed.
Sources of data (documents/ persons)	1)Documents that need to be reviewed or 2)Persons who have to be interviewed
Assessment questions/ Calculation/ The alternative answers	1)Questions to address to the respondents 2)Formula: calculation to be performed that results in a numeric expression of a measure
Standard criteria	Criteria or cut point for conclusions
Results from pilot testing	Description or computation from pilot testing, and the conclusions derived through the assessment
Limitations and recommendations	Description of the limitations for using the indicator and recommendations for the indicator refinement

Detailed description of the developed indicators (Final draft)

Domain 1: Policy, Law, Plan and Structural support

The indicators in this domain could be used to identify the existence of and the relevance of legal provisions, policy, and plans in various levels, and also to examine the organizational structure which includes guidelines, SOPs, protocols, dedicated budget, designated staff, facility infrastructure, and related committees. They reflect the enabling factors to enhance the successful towards the organizational goals. This domain contains 2 subdomains: 1) policy, law, and plans, by which the organization uses to lead its operations, and 2) organizational structure that includes personnel, budget, facility infrastructure such as IT, guidelines, and so on.

Headings	**Descriptions**
Subdomain 1	**Policy, law, and plans**
1.1 (Effectiveness)	A policy statement related to pharmacovigilance (PV)
Purpose	To examine whether a policy exists within the National Drug Policy (NDP) or as a part of other related policy documents with an issue that clearly addresses PV activities
Rationale	A policy statement is the essential document to guide the direction, scope, and activities of PV. It should be developed, usually reviewed, and should especially included in the NDP. Such statements may include those within other related policy documents, such as the Essential Drug Policy. They may be government commitment to fund the PV activities.
Data collection	*Collection frequencies*: Every 5 years *Sources of data:* NDP, National PV policy, MoPH (the Ministry of Public Health) policy documents, other related policy documents *Assessment questions*: 1. Is there a statement of national policy specified on PV? (Y/N) What are they? Please specify. 2.Is there a standard procedure for reviewing the policy? (supplementary) 3.Has the policy been reviewed periodically? (supplementary) *The alternative answers*: Check “YES” if there are policy statements related to PV within the NDP or other policy documents and that policy statement was reviewed periodically. Check “NO” if there is no policy or no policy statement on PV within the NDP and other related policy documents, or if the current one was not recently reviewed.
Standard criteria	Advocacy for PV activities should be provided and available within the national policy documents.
Results from pilot testing	According to the recently adopted NDP statement, one of the strategies of the NDP clearly demonstrated and was prioritized for

	PV activities. The policy statement indicated that safety issue is an essential performance of pharmaceutical system to be achieved. It revealed that PV activities take the vital role in drug safety surveillance and provides safety information to make decision in mitigation of drug risk. The current NDP was approved by the Cabinet in March 2011. Another policy that showed some linkage to PV is the essential drug policy. Some categories in the essential drug lists required health professionals to perform safety surveillance through Drug Utilization Evaluation (DUE).
Limitations and recommendatio-ns	Policy statements may be recently reviewed, but not comprehensive, or they may not be reviewed, but still relevant. Moreover, official commitments from the government, eventhough they are not the declared policies, can be checked "YES". In addition, there are no ways to ensure that such statements are implemented. However, level of accomplishment of the policy stated should be identified as the percentage of the accomplished policy.

1.2 (Effectiveness)	Existence of legal provisions for PV
Purpose	To examine whether current pharmaceutical legislation addresses the aspects of PV.
Rationale	Laws and regulations are some of the most essential elements for PV activities. Regulations are used as the guidances to implement the law. In Thailand, like many regulatory authorities in other countries, various laws and regulations exist to ensure the safety of pharmaceutical products.
Data collection	*Collection frequencies*: Every 5 years *Sources of data:* The Drug Act, pharmaceutical legislation and regulations, other related laws and policy documents *Assessment questions*: 1. Are there legal provisions related to PV? What are they? Please specify. 2. What is the specific act or regulation of the legislation that serves for PV? 3. Does the law connect to the policy previously identified? 4. Has the law been reviewed periodically? How often has it been reviewed? (supplementary) *The alternative answers*: Check "YES" if specific requirements for PV are issued in the laws and regulations. Check "NO" if there is no statement related to PV in any of the laws and regulations.
Standard criteria	Legislation for PV activities should be provided in the country.

Results from pilot testing	PV activities are not stated directly in the laws (mandatory), but voluntary ADR reporting system is in place. However, legal provision through the Safety Monitoring Program (SMP) or related condition has been placed on some products with significant safety concerns, such as new chemical entities. Such products are registered on the specific condition that the MAH has to conduct postmarketing studies related to drug safety or ADR monitoring activities for the marketed medicines.
Limitations and recommendaions	The law may not specifically address PV and may use indirect or broad statements, and only draft legislation may be in place.

1.3 (Effectiveness)	Existence of strategic plans or annual operational plans
Purpose	To identify whether strategic plans or annual operational plans exist and have been implemented.
Rationale	Strategic plan is critical for any organization to guide its goals and achievements in the short or longer periods. Annual operational plan is to guide its commitments to achieve goals, setting in each year, to ensure the effectiveness of the organization.
Data collection	*Collection frequencies*: Annually *Sources of data:* Organizational strategic plan, annual operational plan, and evaluation report documents *Assessment questions*: 1. Is there a strategic plan or annual operational plan for PV activities? Please describe what they are. 2. Are these plans tied up with the policy or laws stated previously? 3. Have the strategic plans and operational plans been reviewed periodically? 4. How have they implemented? *The alternative answers*: Check "YES" if any formal documents of such a plan exist and have been operationalized.
Standard criteria	The document of a strategic plan, and an annual operational plan should be available. Such a plan should have been implemented.
Results from pilot testing	There was no explicit strategic plan for PV development, but annual operational plan has been available and updated every year.
Limitations and recommendatio-ns	The documents of such a plan may exist, but not be operationalized or implemented. This indicator can be seperated as for strategic plan and for operational plan, in order to make better understanding.

Headings	**Descriptions**
Subdomain 2	**Structural support**
1.4 (Effectiveness)	Presence of good oganizational management
Purpose	To identify whether the national PV center has a formal organizational structure and is mandated to handle PV and drug safety issues
Rationale	A PV center has a specific mandate for drug safety surveillance. It would have optimally functioned if an official mandate, roles, and responsibilities have been clearly declared and its organizational structure has been well set up.
Data collection	*Collection frequencies*: Every 5 years *Sources of data:* The Drug Act and related laws, the declaration document for establishment of the national PV center *Assessment questions*: 1. Is there a clear organizational mandate? 2. Is there organizational structure? 3. Is there designated role and responsibility for specific task? *The alternative answers*: Check "YES" if an official document exists with clear mandate, organizational structure, roles, and responsibilities for the national PV center and these details have been operationalized.
Standard criteria	The formal detailed documents for establishment of the national PV center should be available and have been operationalized and implemented. Pharmacovigilance (PV) center should have a clear mandate, structure, roles, and responsibilities.
Results from pilot testing	In Thailand, the NPVC has been well established, and fully operationalized PV activities for nearly 30 years.
Limitations and recommendatio-ns	The PV operations may exist where clearly mandate, roles, and responsibilities have not been mentioned in the official documents. The structure of the organization may not have been well established.

1.5 (Effectiveness)	Human resource management
Purpose	To identify whether there have been staffs assigned a specific responsibility to address PV activities.
Rationale	Having staffs designated for full-time PV activities will facilitate the safety use of medicines in the country.
Data collection	*Collection frequencies*: Annually *Sources of data:* Documents of job description of the PV center *Assessment questions*: 1.Is each staff assigned a specific responsibility? 2.Does the organization evaluate workload and number of staff?

	3.Has the national pharmacovigilance center commissioned the advisory committee or subcommittee or ad hoc working groups responsible for providing technical advice on medicine safety issue? How were the members of the committee or the working group recruited? *The alternative answers*: Check "YES" if someone is responsible for PV and job descriptions indicate the roles and responsibilities for PV activities.
Standard criteria	Job description of specific PV responsibility should be provided, and announced for the designated staff.
Results from pilot testing	PV activities are part of the job description of the Technical and Planning division, ThaiFDA. The NPVC, under the auspices of such division, has been established to operationalize PV activities at the national level. *Note: question 2 and 3 have not been tested*.
Limitations and recommendatio-ns	PV activities may be the parts of job descriptions of the drug control unit/ division or any other divisions. Efforts should be made to clarify the responsibility to the persons in charged.

1.6 (Effectiveness)	Dedicated budget available for PV-related activities
Purpose	To investigate whether the budgetary allocations have been provided annually to the center for its activities.
Rationale	For sustainable development of PV activities, the government should commit funds toward safety surveillance. An annual budget should be appropriate and sufficient for the operation of plans related to safety of medicines.
Data collection	*Collection frequencies*: Annually *Sources of data:* Budget allocation documents *Assessment questions*: 1. Is there a specific budgetary allocation for annually planned PV activities? 2. Is the budget sufficient for each of the planned activities? *The alternative answers*: Check "YES" if the government supports financial resources required for the functioning of the national PV center.
Standard criteria	The government should provide annually appropriated funding for the center to support its activities.
Results from pilot testing	The government always provides financial support for PV activities through the NPVC fiscal budgetary plan.
Limitations and recommendatio-ns	Assessment should include the sufficiency and appropriateness of the budgetary allocations.

1.7 (Effectiveness)	Existence of a system to facilitate drug safety surveillance
Purpose	To investigate whether facilitating infrastructure are in place. These include the national guidelines or SOPs that provide operational standards for PV activities such as spontaneous reporting flow, roles and responsibilities of stakeholders; a standard form for collecting and reporting ADR related to suspected medicines from healthcare workers and others; and IT for PV data to be processed and stored.
Rationale	National PV guidelines provide directions, definitions, and operational standards of the approaches and processes for ADR reporting and drug safety monitoring. They help harmonize understanding and approaches for PV activities in the country. Also, a harmonized form used for ADR reporting and any other PV related data is one of the critical parts for PV development. Moreover, effective collaboration of all PV data collection at the national center will enhance further data processing and data analysis for signal generation.
Data collection	*Collection frequencies*: Annually *Sources of data:* National PV guideline documents, database review, sample of ADR reports received, other related documents. *Assessment questions*: 1.Is there a standard operating procedure/guideline for staff at National PV center to follow? 2.Is there a standard operating procedure/guideline for ADR reporters to follow? 3.Is there standard form for PV data collection? 4.Does the national pharmacovigilance center have (workable) hardware and software to manage data? 5.Is there an IT maintenance system ? *The alternative answers*: Check "YES" if a system or strategy exists to facilitate drug safety surveillance.
Standard criteria	National PV guidelines should be available and periodically revised. Any forms for ADR or drug safety issue reporting should be developed and routinely used in the locations of data providers. They should be revised to ensure the consistency with international standards and the requirements for data analysis. In addition, ADR or other PV data warehouse that contains data from all sources, as well as IT system should be developed.
Results from pilot testing	A comprehensive guideline, as well as a standard form for ADR reporting has been developed and available at health institutes.
Limitations and recommendations	The guidelines may not mean only how to collect and record ADR report, but they should address all issues related to PV in the country. For a standard form, it should be revised through

	consensus of data providers to enhance the acceptance for the form being used. Data fields should be revised to ensure that needed and sufficient data are collected and filed.

1.8 (Effectiveness)	Existence of PV national forums
Purpose	To investigate whether platforms and/or forums exist for the coordination of PV activities across all stakeholders
Rationale	PV involves several stakeholders such as healthcare providers, pharmaceutical industry, patients, professional associations, etc. The national forums for coordination of PV activities are essential to enhance mutual understanding through opened-mind communication and clearly speaking out.
Data collection	*Collection frequencies*: Annually *Sources of data:* Reports of work accomplishment *Assessment questions*: 1.Does the national pharmacovigilance center arrange a platform or forum that all stakeholders may attend? 2.How often have the forums been held? How many people attend the forum? 3 Is there any issue being generated from the forum? Whether there is any action taken for those issues? *The alternative answers:* Check "YES" if a formal forum for coordination of PV activities has taken place in the last year.
Standard criteria	A formal forum for PV coordination should be conducted at least once a year.
Results from pilot testing	The NPVC always arranges a coordination forum twice a year.
Limitations and recommendations	Definition of coordination of activities should be clarified and stakeholders' map should be developed and periodically revised.

1.9 (Effectiveness)	Existence of an ADR or drug safety advisory committee or a subcommittee with a functional activity related to PV
Purpose	To identify whether a national drug safety advisory committee exists and has been functioning.
Rationale	A national ADR or drug safety advisory committee provides technical advice on the safety of medicines to the regulatory authority and the national PV center to make decisions about drug-related risk management.
Data collection	*Collection frequencies*: Annually *Sources of data:* The Drug Act and related laws and regulations; minutes of the national drug safety advisory committee meetings

	Assessment questions: 1. Does an ADR or drug safety advisory committee or a subcommittee exist to provide technical advice to the ThaiFDA on drug safety issues? 2. Does the committee or subcommittee meet regularly or at least once a year? *The alternative answers:* Check "YES" if there are official documents constituting a national drug safety advisory committee, and records of such the committee confirm meeting at least once within a year.
Standard criteria	Such a committee should be advocated for the establishment, and developing terms of reference for its mandate should be supported.
Results from pilot testing	At the national level, Drug safety advisory subcommittee has been appointed by Drug committee. The subcommittee provides data relevant to safety issue and recommends corrective or regulatory actions for decision making to minimize risk.
Limitations and recommendations	The committee may exist, but not function.

Domain 2: Safety surveillance

One of the major roles of the NPVC is to monitor safety information of both those occurred in the boundary of Thailand and in the global level. The indicators in this domain reflect the capability of the organization to participate and build partnerships, and bring multiple stakeholders together for successful information exchange. It refers to the coordination and collation of data between data providers and the national center (NPVC), timely and effective data flow, as well as the quality of data obtained from secondary sources. This domain contains 2 subdomains: 1) the function of the NPVC to provide safety surveillance in the country, and 2) the function to monitor safety information from the secondary sources such as Drug Regulatory Authority (DRA) in other countries, corresponding news, e.g. BBC, CNN, etc.

Headings	**Descriptions**
Subdomain 1	**Safety surveillance within the country**
2.1 (Effectiveness)	Percentage of health institutes contributing in PV activity
Purpose	To determine how many of health institutes submitted ADR reports to the NPVC in a given year
Rationale	Health institutes are the major sources for the data of Drug-ADR pairs in every countries. These data are the essential raw materials to generate safety signal. Many types of settings have contributed in this activity through the monitoring and reporting system, via two main channels; hard copies and electronic submission.

Data collection	*Collection frequencies*: Annually *Sources of data:* Database review, documents of the MoPH statistics unit (for number of health institutes in the country) *Assessment questions*: How many percent of health institutes summitted ADR report? Analysis can be conducted on:- 1)**types of settings**: Percentage of health institutes (reporting sources) with functional PV activity (submitting >= 1 report annually to the NPVC) 2)**geographic areas**: Percentage of health institutes (reporting sources) in each region with functional PV activity (submitting >= 1 report annually to the NPVC) 3)**types of settings by channel of report submission**: Percentage of hardcopy reporting sources and those of electronic sources *Note:* (1)functional PV activity means submit >= 1 report in a given year. (2)types of health institutes include:- (2.1) public hospitals (2.2) private hospitals (2.3) health centres and other institutes (2.4) community pharmacy / drug store (2.5) MAH / registered pharmaceutical manufacturing industry (voluntary reporting) (3)geographic areas include:- BKK, the vicinity of BKK, northern, southern, northeastern, western, eastern, and central part of Thailand *Calculation:* 1) number of health institutes submitting >=1 report in a given year (a), total number of each types of health institutes or number in each region (b) Formula:- (a)/(b)×100 2) number of reporting sources submitting reports via electronic (a), those submitting via hardcopies (b) Formula:- (a)/(a+b)×100, and (b)/(a+b)×100
Standard criteria	1)100 percent of health institutes are expected to contribute. 2)100 percent are expected to submit reports via electronic submission.
Results from pilot testing	*Data has not been collected.*
Limitations and recommendatio-ns	Data should be collected for several years in order to see time-trend and analyzed for improving the weak parts.

2.2 (Effectiveness)	ADR reporting rate
Purpose	To determine reporting rate by comparing the number of ADR reports received in a given year to number of million population
Rationale	ADR reports are collected for further analysis to be an information source for decision making in risk management. ADR reporting rate can be used as the PV targeted goal, when comparing to other countries in different size of population or even within a country by consideration of different size of population in each region.
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review, documents of the national statistics department of Thailand (for the number of midyear population) *Assessment questions*: 1) Number of reports received in a given year per number of million population for the whole country; midyear population *Note*: Analysis can be conducted as a supplementary measurement on:- Number of reports received in a given year per million inhabitants in each region (BKK/ vicinity of BKK/ north/ south/ north-east/ west/ east/ central part of Thailand) *Calculation:* 1)Number of ADR reports received in a given year (a), number of million population; midyear statistics (b) Formula:- (a)/(b)
Standard criteria	No standard criteria are available.
Results from pilot testing	*Data has not been collected.*
Limitations and recommendatio-ns	Data should be collected for several years to see time-trend.

2.3 (Effectiveness)	Ratio of specific types of ADR report and total reports
Purpose	To investigate some specific types of reports that are more considerably concerned
Rationale	Some types of ADR should be more awared according to its impact to the safety concern either on the individual patients or in the larger society. These include ADRs that related to novel medicines and serious case reports.
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review *Assessment questions*:

	1) Number of serious ICSRs (Individual Case Safety Reports) per total number of reports received in a given year 2) Number of suspected new drug-ADR reports per total number of reports received in a given year *Note*: new drug means drug registered not more than 5 years. 3) Number of reported drug items in SMP per total number of SMP drug items in a given year *Calculation:* 1)Number of serious ICSRs (a) or suspected new drug-ADR reports (b), total number of reports received in a given year (c) Formula:- (a)/(c), or (b)/(c) 2)Number of reported drug items in SMP (d), total number of SMP drug items in a given year (e) Formula:- (d)/(e)
Standard criteria	1)No standard criteria are available for reporting rate of serious ICSRs or ADRs related to new drugs. 2)All of SMP drug items are expected to be reported.
Results from pilot testing	*Data has not been collected.*
Limitations and recommendatio-ns	Data should be collected for time-series analysis. For SMP drug lists, it is difficult to link data from Drug Control Division, which is in charge of the registration of new chemical entities and responsible for SMP. The problem dues to the poor data management system within the ThaiFDA.

2.4 (Efficiency)	Compliance with time requirement for ADR report submission
Purpose	To determine how many of ADR reports submitted within time requirement
Rationale	According to the standard procedure stated in domestic PV guideline, health institutes are encouraged to report all types of ADR, especially serious events, to the NPVC. Fatal or life-threatening event requires immediate reporting, either by telephone, faximile, e-mail, or in writing; or within 48 hours after detection. SUSARs case requires reporting within 15 calendar days, and for serious, but labeled or other non-serious symtoms require reporting within 2 months. Speed or lead time reflects the efficiency of the NPVC to generate signal earlier and in timely manner.
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review *Assessment questions*: How many of ADR reports submitted within time requirement? 1)Percentage of ADR report with death case submitted within time requirement (48 hrs after detected) 2)How frequently ADR reports submitted annually?

	Note: (1)For hard copies, considered time means time during date of ADR detection and report arrival date at the NPVC (2)Analysis can be conducted on:- (2.1) hard copies (2.2) electronic submission *Calculation:* 1)Number of ADR reports with death case submitted within time requirement (a), total number of submitted reports in a given year (b). Formula:- (a)/(b)×100 2)Annual frequencies the reporting providers submitted ADR reports (1-2 times a year/ 3-4 times a year/ 5-6 times a year/ > 6 times a year)
Standard criteria	1)100 percent of ADR reports with death case are expected to be submitted within time requirement. 2)All of ADR reports are expected to be submitted to the NPVC not less than 6 times a year.
Results from pilot testing	*Data has not been collected.*
Limitations and recommendatio-ns	It is difficult to determine whether a report is submitted within time requirement. Hence, practicability of this indicator is quite low.

Headings	**Descriptions**
Subdomain 2	**Safety surveillance from secondary sources (e.g. DRA website, corresponding news)**
2.5 (Efficiency)	Monitoring of drug safety information from secondary sources
Purpose	To determine how efficiently the NPVC acquired safety information from other sources outside the country
Rationale	Safety surveillance from secondary sources is one of the essential functions of the NPVC. It enhances the NPVC to acquire important information efficiently. The performance of this function can be determined through the frequencies in monitoring safety information, and the provision of supporting information regarding the magnitude of risk, or other important information.
Data collection	*Collection frequencies*: Annually *Sources of data:* Chief and staff of the NPVC, reports of work accomplishment *Assessment questions*: 1)How frequently the assigned staff monitor safety information from specified secondary sources? (every day/ every 2 days/ every

	week/ >every week) 2)If the risk or safety information from secondary sources is not clear, did the assigned staff acquire supporting information regarding the magnitude of risk or statistical results or other important information? *The alternative answers:* Check "YES" if the assigned staff acquired supporting information when the information from secondary sources is not clear.
Standard criteria	The assigned staff is expected to monitor safety information from secondary sources every day, and also acquire additional important information when the information from specified sources is not clear.
Results from pilot testing	The function of the NPVC to monitor safety information from other sources outside the country has been well established. The specified staff is circulatedly assigned to monitor safety information from credible sources every day.
Limitations and recommendations	Assessment should include the use of such information acquired from secondary sources.

Domain 3: Signal detection and decision making for risk management

This domain refers to the function of the NC to collect, summarize, and transform of ADR information; to identify, estimate, and evaluate the volume and seriousness of risks that associated with a pharmaceutical product; and to propose the corrective measures to minimize risks. 4 main indicators, as the followings; capability to prepare data ready to be analyzed; quality of data acquired (in-house database); automated signal detection; and decision making for risk management, were developed. They reflect the capability of the organization to manage large dataset in order to generate drug safety signal and make decisions for risk management.

Headings	**Descriptions**
3.1 (Effectiveness and Efficiency)	Capability to prepare data ready to be analyzed
Purpose	To identify the capability of staff on report verification
Rationale	Report verification is the important procedure to ensure the accuracy of PV data acquired. Verified data are ready to be further processing.
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review, Workload review *Assessment questions*:

	1.Percentage of reports in the database that have been verified? (Effectiveness) 2.How efficiently the responsible staff work on verifying new coming reports? (Efficiency) *Note*: This indicator is used in pre-data processing check of reports. *Calculation:* 1.Number of verified reports (a), number of total reports in the database (b) Formula:- (a)/(b)×100 2.Calculate output/ input (full-time equivalent): if the calculated answer <1, it means "not efficiency"; the optimal efficiency is equal to 0(zero).
Standard criteria	1)100 percent of reports in the database are expected to be verified 2)There is no standard criteria available to determine workload.
Results from pilot testing	*Data have not been collected.*
Limitations and recommendations	It is sophisticated task and may be take some time to collect data for calculation of workload.

3.2 (Efficiency)	Quality of data acquired (in-house database) (This indicators were derived from the WHO-UMC)
Purpose	To identify the quality of data acquired from ADR reporting system and stored in the national database (ThaiVigibase)
Rationale	"Quality of data means the degree to which the recorded data is representative of the original information. Good data quality management is cost reduction, e.g. the cost of recall, repair, or rework of the faulty information as compared with the information that work satisfactorily" (Lindquist, 2004).
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review *Assessment questions*: 1.**Report completeness**-Percentage of key data fields that were filled in (quantitative measurement): This indicator was designed as a sum of scores for defined key data fields to measure the overall completeness of each report, e.g. 70 percent of the key fields were filled in. 2.**Missing data**-Key data items that were often not filled in (qualitative measurement): *Note*: "often" must be clarified. This indicator was designed to check the data items that were often missing. 3.**Data accuracy or incorrect translation**-Percentage of data fields that the reported values matched predefined values in

	translated terminologies or look-up tables: This indicator was designed to check of filled-in values in each data field against predefined values in the corresponding controlled or translated terminologies. 4.**Data consistency**-Percentage of logically linked fields that the reported information were in conflict: This indicator was designed to check of a field-field comparison with predefined logical checks. Examples of consistency checks were as the followings; date of onset must not be before start of treatment with suspected drug; pregnancy must be women only. *Calculation:* Percentage of the individual measurement, out of the total data units (data fields or number of reports) *Note*: Analysis can be conducted on:- 1) hardcopies 2) electronic submission
Standard criteria	No standard criteria are available now.
Results from pilot testing	*Data have not been collected.*
Limitations and recommendations	Due to the sophisticated structure of PV database, it is difficult to collect data to fulfil this indicator. Unit of analysis must be clarified whether the computed number are at report level or data element level.

3.3 (Effectiveness)	Automated signal detection
Purpose	To identify whether potential signal has been completely reviewed and analyzed
Rationale	Signal generation is one of the main objectives to execute PV activities. Automatic tool helps the NPVC manage large dataset effectively. The potential signal generated should be further reviewed and analyzed as soon as possible.
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review, Minutes of the Signal Review Panel meetings *Assessment questions*: Percentage of potential signals that have been completely reviewed and analyzed *Calculation:* Number of potential signals that have been reviewed (a), number of potential signals generated (b) Formula:- (a)/(b)×100 *Note*: Serious cases can be sub-analysis.
Standard criteria	100 percent of potential signals generated by automated tool are expected to be reviewed and proposed for risk management.
Results from	*Data have not been collected.*

pilot testing	
Limitations and recommendations	Some signals are known and not serious. For these situations, the review panel should set priority and decide what need to be reviewed accordingly.

3.4 (Efficiency)	Decision making for risk management
Purpose	To identify whether the subcommittee is functioning efficiently
Rationale	"In pharmacovigilance, making the right decisions at the right time is critical" (Lindquist, 2004). Drug safety advisory subcommittee, composed of technical experts and academicians from various fields, is responsible for technical advice in making decision about the corrective measures to manage risk. The efficient process for work accomplishment of the subcommittee reflects the capability of the NPVC as the secretariate of the subcommittee.
Data collection	*Collection frequencies*: Annually *Sources of data:* Minutes of the national drug safety advisory subcommittee meetings *Assessment questions*: 1. How often does the subcommittee meet? 2. Are there any standard criteria for the subcommittee using in making the decision? 3. Lead time spending on decision making through the advisory subcommittee *The alternative answers:* Average lead time from safety issue emerging date to date of decision making (days / weeks / months) *Note*: Analysis can be conducted on:- 1) serious cases 2) non-serious cases
Standard criteria	Criteria for the subcommittee using as the principle in decision making should be developed. For lead time spending on making decision, there have been no standard criteria available.
Results from pilot testing	*Data have not been collected.*
Limitations and recommendations	Lead time spending on different issues may vary considerably, due to the sufficiency or the quality of the available information.

Domain 4: Communication of safety information

The indicators in this domain reflects the capability of the organization to organize timely and effective dissemination of safety information, and its responsiveness to any related queries either in domestic level or international level in order to facilitate safety surveillance. 3 core indicators have been developed as the followings:-

Headings	**Descriptions**
4.1 (Effectiveness)	Effectiveness of safety information communication
Purpose	To identify how effectively the NPVC is performing in communication
Rationale	Good communication practice includes providing right information (accuracy) at the right time (timeliness) to the right audiences (targeted).
Data collection	*Collection frequencies*: Annually *Sources of data:* Documents of the NPVC such as plans, SOPs *Assessment questions*: 1.Does the NPVC communicate safety information to its targeted audiences? Please specify who is the targeted audiences. (e.g.health professionals / the MAHs / general public, etc.) 2.Does the NPVC utilize a variety of channel for communication? Please specify. What is the most functioning channel? 3.How fast the information has been distributed? *Note*: Analysis can be conducted on serious or non-serious information. *The alternative answers:* Average lead time from safety issue generating date to date of dissemination are calculated to determine how fast the information are disseminated.
Standard criteria	No standard criteria are available for speed of communication. However, the information are expected to be disseminted to all targeted audiences.
Results from pilot testing	*Data have not been collected.*
Limitations and recommendations	This indicator does not reflect quality of the content of information disseminated or what extent of satisfaction of the audiences who received the messege.

4.2 (Effectiveness)	Knowledge sharing
Purpose	To identify how effectively the NPVC performs knowledge sharing
Rationale	Sharing of knowledge emerged from safety information with

	various key stakeholders including health professionals and consumers will enhance the generating of new safety signals and alerts that should be communicated properly and rapidly.
Data collection	*Collection frequencies*: Annually *Sources of data:* Publication review on the national and international related journals, other related documents *Assessment questions*: 1. Is there a publication authored by at least one of the NPVC staff existing in the PV related journals? How many of the publications in a year? Please specify the topics which have been published. 2. Has public education conference or academic seminar been held to transfer knowledge from the NPVC to other institutes? If so, how often the conference or seminar has been held? Who attended? Please specify the topics discussed. *The alternative answers:* Check "YES" if a publication authored by at least one of the NPVC staff involving a PV related topic exists, or a conference or seminar has been held.
Standard criteria	No standard criteria are available.
Results from pilot testing	*Data have not been collected.*
Limitations and recommendations	This indicator does not identify the credibility of the journals, or subsequent activities drawn from the discussed topics.

4.3 (Effectiveness)	Response to external inquiries
Purpose	To identify how effectively the NPVC responds to external inquiries either from health professionals or the general public
Rationale	Drug safety alerts and warnings may be communicated through various channels. Provision of drug safety information that responses to any inquiries is an essential strategy to promote safe use of medicines.
Data collection	*Collection frequencies*: Annually *Sources of data:* Database review, reports of work accomplishment *Assessment questions*: 1. Is there the query-response service existing in the NPVC? If so, how many of communication channels providing the activity? Please specify. 2. Is there an assigned staff responsible for this job? 3. Percentage of questions or inquiries that have been answered or fed back 4. What is the average responding time? Note: Analysis can be conducted regarding groups of people to be

	responded. *The alternative answers*: Check "YES" if the query-response service exists at the NPVC.
Standard criteria	100 percent of the queries are expected to be responded. However, no standard criteria are available for responding time.
Results from pilot testing	*Data has not been collected.*
Limitations and recommendations	The details of any queries should be periodically reviewed and further analyzed to better problem solving.

Appendix B

Framework for organizational assessment (draft 1)

the proposed indicators

1. Data management of individual case reports of ADRs

Objective: to collect, update, summarize and transform of ADR information

Structure	**Process**	**Output**
1.percentage of hospitals/clinics/pharmacies reporting ADR events to the national centre compared to all hospitals/clinics/pharmacies in Thailand -public hospitals -private hospitals -clinics -pharmacies 2.percentage of ADR data received from all sources (hospitals, clinics, pharmacies, health centers, etc.) 3.mean durations from ADR detection in each source to data sending to the national centre 4.number of rejected reports each year 5.regular errors found during data recording process 6.number of reports received per month, per year 7.reporting form : user friendly?, comprehensive?,	1.mean time for data entry (key in process) 2.mean time for data verification 3.frequencies for data "back-up" 4.mean time for "Annual summary" content preparation and publication	1.percentage of drug related adverse events compared to all drugs registered in Thailand 2.coverage of "Annual summary" distribution -per sources of data received -per healthcare personnel

relevant? 8.needed data for individual case reports : completeness?, currency?, accuracy?, relevant? 9.data “back-up” system : “Firewall”?, “virus” detection and prevention?, confidentiality?, accessing level?		

1.2 Signal detection, risk identification, and risk assessment

Objective: to identify, estimate, and evaluate the volume and seriousness of risk that associated with a pharmaceutical product

Structure	**Process**	**Output**
1.automatic tool : user friendly?, easy for maintenance?, easy to upgrade or re-innovated?, “virus” detection and protection?, “firewall”?, frequencies for program maintenance? 2.experts for clinical judgment : available?, accessible?, sufficient? 3.member of “Signal review panel” : functional?, active?, participatory?	1.frequencies for running “Automatic tool” 2.mean time for each running 3.significant errors found in running process 4.mean time for reviewing each drug-ADR combination 5.number of drug-ADR combination reviewed each year 6.frequencies for “Signal review panel” meeting each year	1.number of “Potential Signal” generated each year 2.number of “Signal” strengthened and entered the ADR advisory committee to make decisions

1.3 Decision making procedure to consider risk minimization tools

Objective: to propose actions to minimize risk

Structure	Process	Output
1.number of the committee's members 2.educational degree of the members 3.mean times each members came to participate the meetings 4.risk information : trust?, accessible?, adequate?, rapid?, up-to-date?	1.frequencies of the committee's meetings each year 2.mean time spending in each meeting 3.mean time spending to prepare for each meeting (including searching for essential information, preparing invitation letter, writing reports, arranging facilities for the meetings, co-ordinating members of the committee, etc)	1.cumulative number of regulatory actions in each category proposed by the ADR advisory committee since the starting year 2.compliance of the proposed actions in Thailand compared to other countries'

4. Risk communication, and dissemination of risk minimization tools

Objective: to prepare contents and disseminate information about drug risk and/or risk mitigation tools to various stakeholders

Structure	Process	Output
1.lists of the authors regularly contributed for the contents of publications. 2.contents of the publications : interesting?, up-to-date?, consistency?, accuracy?	1.mean time spending for preparing each chapter 2.frequencies of issuing each year 3.mean time for publishing process 4.mean time of late issues occurred	1.number of audiences receiving the publications 2.number of institutions receiving the publications 3.mean number of web-based access each month 4.number and quality characteristics of people participated in exchanging information via mail box

Appendix C

Summary of the developed indicators (Draft 2)

Function of the organization		Effectiveness	Efficiency	Related factors
	Plan and policy	1. Are there …….. for PV. activities? 1) legislative provision 2) national policy document 3) strategic plan document 4) annual operational plan 2. What are they? 3. How have they implemented?		strategic leadership, structure, stakeholder, political environment
Acquiring data input	Ordinary drug items	1.1 Reporting rate / million inhabitants 1) the whole country 2)geographic areas 1.2 Ratio of reports submitted by hospitals in each level (regional/ provincial/ district/ medical school/ private hospitals)	1. Reporting rate per number of health professional (pharmacists) 1) the whole country 2) geographic areas 2.Average lead time from ADR detected date to report submitting date (electronic)	human resources, incentives, infrastructure

			3.Annual frequencies that reporting providers submit reports to the NC (hard copies)	
		2. Percentage of health institutes contributing in PV activity 1) types of setting 2) geographic areas 3) channel of reporting	1. Percentage of reporting providers submitting reports with time requirement 1) death cases within 48 hrs after detected (see page 2) serious, and non-labeled cases within 15 calendar days 3) other cases within 2 months	human resources, incentives, infrastructure, technology
	SMP drug items	3.Percentage of drug items submitted ADR reports / total number of SMP drug items in a particular year		infrastructure, technology
	Secondary sources of data input		1. Are drug safety information sources easily accessible? 2. Is there any criterion for selecting drug safety information sources to ensure the credible information? If so, what is it? 3.Ratio of safety information from	human resources, technology

			primary sources (in-house database) and secondary sources determined by the advisory committee annually	
	Data quality		1. completeness 2. missing important data 3. syntactic inaccuracy 4. semantic inaccuracy 5. incorrect translation 6. inconsistency	human resources, incentives, infrastructure, technology
Data processing	Data key-in (hard copies) Data verification (hard copies) Data processing	1.Proportion of volume of reports key-in and volume of reports received annually (hard copies) 2.Proportion of volume of reports verification and volume of reports key-in annually (hard copies)	1.Average lead time 1) from data received date to data entry date (hard copies) 2) from data entry date to data verification date (hard copies) 3) from data verification date to data processing date by automated signal generation (hard copies)	human resources, incentives, infrastructure, technology
Data analysis		1.Proportion of number of potential signal generated annually (old signal /		technology, knowledge (of human)

		new signal) 1) from in-house database 2) from secondary sources		
Decision making for risk minimization strategies		1.Proportion of number of safety issues emerged and number of work accomplished annually (decision for actions under the advisory committee's consideration)	1.Average lead time 1) from safety issues emerged date to date for dissemination of information (in-house database / secondary sources) 2) from safety issues emerged date to date of decision making for actions (through advisory committee)	availability and accessibility of experts, technology to access safety information, stakeholders
Communication of safety information		1. Proportion of information accessed, out of the information provided in the website (www.fda.moph.go.th/ vigilance) in a given month		technology, human resources
		2. Number of publication in the related journals per number of staffs (pharmacists) in a given year		human resources

Appendix D

GLOSSARY OF TERMS

Accountability is the obligation to account for one's conduct and actions, usually to an individual or group, but ultimately to the public. Both individuals and organizations may be accountable.

Adverse Drug Reactions (ADRs) is defined as any response to a drug that is noxious and unintended, and that occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function, and usually occurs within a reasonable time after administration of the drug; ordinarily, therapeutic failures, unintentional or accidental overdose, or misuse are excluded.

Adverse event is any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment.

Assessment is often used as a synonym for evaluation; sometimes recommended for approaches that report measurement without making judgments on the measurements.

Causality assessment is the determination of whether a reasonable possibility exists that the product is etiologically related to the adverse experience.

Effectiveness is an expression of the degree and extent to which planned activities are realized and planned results achieved.

Efficiency is the relationship between the results of activities and the corresponding effort expended in terms of money, resources and time.

Evaluation is a time-bound exercise that attempts to assess systematically and objectively the relevance, performance and success of ongoing and completed programs and projects (UNDP, 1997).

Harm is damage qualified by measures of frequency of occurrence, severity or duration.

Hazard is the potential source of harm.

Indicator is commonly described as a person, thing, or device that measures, records, or declares something. Indicators can be thought of as pieces of information that provide evidence on matters of broader concern. Indicators should meet the criteria of clarity, usefulness, measurability, reliability, validity, and acceptance by key stakeholders.

Input refers to the amount of resources has been used, such as expenditures or employees.

Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Monitoring is a continuing function that aims primarily to provide program or project management and the main stakeholders of an ongoing program or project with early indications of progress or lack thereof in the achievement of program or project objectives (UNDP, 1997).

Organization is defined as formalized entities that involve a cluster of people who are brought together for a common purpose. They include a wide spectrum of human activity and can be categorized as private or public, for-profit or non-profit, governmental or nongovernmental, and so forth.

Outcome refers to the result of an agency's output, and are generally divided into two categories: intermediate and final outcome. Intermediate outcomes are the progression toward a final outcome, such as a change in behavior or other results that contribute to the end outcome. Final outcomes are the ultimate results the program is designed to achieve, such as an improvement in patient's quality of life, a reduction in pollution emission.

Output refers to the events, products or services produced from the program activities, and delivered or completed during a certain period.

Performance has been defined as results of the organization's management of its activities.

Performance dimensions or domains are broad areas of interest or themes that align with and are designed to capture organizational purposes and functions.

Performance indicators is defined as a specific numerical/ quantitative measurement for each aspect of performance (e.g. output and outcome) under consideration (Hatry, the International City/ Council Management Association, 1999: 13).

Performance measures are qualitative and /or quantitative standards or measures against defined objectives. Performance measures describe major duties, assignments and objectives in terms of complexity, accountability, and results, and should be specific, measurable, attainable and relevant.

Pharmacoepidemiology is the study of the use and the effects of drugs in large numbers of people.

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects to medicines or any other possible drug-related problems (WHO, 2002).

Postmarketing safety surveillance is the study of drug use and drug effects after release onto the market.

Program refers to a group of related projects, services and activities directed to the achievement of specific goals.

Program evaluation is a set of philosophies and techniques to determine if a program works.

Project is a planned undertaking designed to achieve certain specific objectives within a given budget and a specified period of time.

Qualitative data is the data that use non-numeric information for description. Generally words, but may include photographs and films, audio recordings, and artifacts.

Quality is the degree to which a set of characteristics fulfils the requirements.

Quality of data is the degree to which the recorded data is representative of the original information (Lindquist M, 2004).

Quantitative data is the data that describes, explains and reports on phenomena using numbers.

Reliability is an expression of the degree to which a measurement performed by different people at different times and under different circumstances produces the same results.

Risk is the probability of developing an outcome.

Note (1): the term "risk" normally, but not always, refers to a negative outcome.

Note (2): contrary to "harm", the concept of risk does not involve severity of an outcome.

Risk analysis is the systematic use of available information to identify hazards and to estimate the risk.

Risk assessment is overall process comprising a risk analysis and risk evaluation.

Risk control is the process through which decisions are reached and protective measures are implemented for reducing risks to, or maintaining risks within specified levels.

Risk evaluation is judgment, on the basis of risk analysis, of whether a risk which is acceptable, has been achieved in a given context based on the current values of society.

Risk management is defined as the systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, and controlling risk.

Side effect is any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to the pharmacological properties of the drug.

Signal is the reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information.

Spontaneous reporting refers to system whereby case reports of adverse drug events are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority.

Structure refers to external environment and internal factors (inputs) that include time, staff, funding, materials, equipment and others that contribute to an activity. When considered together with outcomes, inputs can be used to determine the level of effort required to achieve an outcome. Inputs are important components for determining efficiency and return on investment of the program.

Unexpected adverse reaction is an adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from characteristics of the drug.

Unit of analysis is the actual object being investigated (e.g., persons, classrooms, organizations, nations).

Validity is an expression of the degree to which a measurement performed actually measures the characteristic which the investigator wishes to measure.

Variable is a characteristic that can assume any one of a range of values.

BIOGRAPHY

Miss Wanida Kaewpanukrungsi was born in Bangkok. She received Bachlor degree of Science in Pharmacy from Chulalongkorn University in 1988, and Bachlor of Law from Sukhothaithammathirat Open University in 2005. She also received two Master degree from Chulalongkorn University: Master of Public Administration in 1996, and Master of Science (Health Economics) in 2000. She started her career with two private companies: the Yaowarach Co., Ltd., as the quality control pharmacist in laboratory of the pharmaceutical factory, and then, the East Asiatic Co., Ltd., as the registration pharmacist. After two year working in private sector, she then moved to work as a government official at the Food and Drug Administration (ThaiFDA). She has been working there for 21 years. At present, her position is a senior pharmacist at the Health Product Vigilance Center (HPVC), the Technical and Planning Division. Her jobs deal with all aspects of pharmacovigilance and health product safety surveillance. She is also interested in management sciences, public policy, and policy analysis.