[emblem]

The Announcement of Food and Drug Administration

Title: Guidance for Market Authorization Holders on Post-Marketing Safety Reporting for Human Drugs, Narcotics, and Medicinal Neuropsychotropic Substances

In order to provide the single direction and standard as well as the definite working procedure of post-marketing adverse events reporting and monitoring related to health products to Market Authorization Holders consequence to their compliance and optimizing the pharmacovigilance effectiveness, therefore Food and Drug Administration of Thailand has been issued the announcement entitled “Guidance for Market Authorization Holders on Post-Marketing Safety Reporting for Human Drugs, Narcotics, and Medicinal Neuropsychotropic Substances” as detail enclosed.

Hence, this will be effective from now on.

The announcement on 18 December 2015

[signature]

(Mr. Boonchai Somboonsook)

General Secretary of Food and Drug Administration

The enclosure of

the Announcement of Food and Drug Administration

Title

Guidance for Market Authorization Holders on

Post-Marketing Safety Reporting for

Human Drugs, Narcotics, and Medicinal Neuropsychotropic Substances

Dated 18 December 2015

Table of Contents

"Guidance for Market Authorization Holders on Post-Marketing Safety Reporting for Human Drugs, Narcotics, and Medicinal Neuropsychotropic Substances"

1. Introduction

Although drugs approved by the Thai FDA have undergone extensive studies on efficacy and safety, from preclinical testing to clinical trials in phases I-III, there are still adverse reactions that are not detected during these studies, and are known only after marketing. This is the result of limitations in clinical studies, e.g. small number of patients, exclusion of children, the elderly and pregnant women as well as patients with liver or kidney abnormalities, and short duration of study. Therefore, reporting and monitoring of adverse drug reactions following the marketing of a drug is crucial to pharmacovigilance and is the responsibility of all parties especially market authorization holders (MAHs). In order to conduct in the same direction, the Thai FDA thus imposed the guidance for MAHs on post-marketing safety reporting of human drug, biological product including vaccine in July 2011. However, the scope of safety issue has been more extensive including the inclusion of medication error as well as lack of effect into drug safety report by European Medicines Agency (EMA). Hence, such guidance does not cover the overall drug safety issues.

In order to improve effectiveness and to provide the standard of health product pharmacovigilance, the Thai FDA in cooperation with the Pharmaceutical Research and Manufacturers Association (PReMA), the Thai Pharmaceutical Manufacturers Association (TPMA), and the Regulatory Affairs Pharmacy Association of Thailand (RAPAT) has updated "the guidance for MAHs on post-marketing safety reporting of human drug, biological product including vaccine".

2. Purpose

This document serves as a guide for MAHs to submit health product safety reports to Health Product Vigilance Center (HPVC), Thai FDA, Ministry of Public Health. In addition, this guidance intends to improve effectiveness, to provide the standard of safety reporting, and to cover all safety issues concerned. The content is including purpose, reporting scope, responsible person, source of occurrence, source of reports, reporting requirements, other drug related-problems, minimum criteria for reporting, reporting time frame, how to report, follow-up reports, other safety reports, reporting flow chart, Thai FDA safety report form, CIOMS form, risk management plan, and glossary.

3. Reporting scope

This document is to provide the guideline for MAHs to submit safety reports of the following drugs:

3.1 Conventional and traditional medicines for human use approved to be marketed, e.g. chemical drugs, biological products, vaccines, and Thai traditional medicines

3.2 Medicine for compassionate use (Nor.Yor.Mor. 4) (refer to the definition in glossary)

3.3 Narcotics and Medicinal Neuropsychotropic Substances

4. Responsible person

The person who is responsible to submit report is categorized according to the drug classification as follow:

4.1 Conventional and traditional medicines for human use approved to be marketed (chemical drugs, biological products, vaccines, and Thai traditional medicines): the responsible person is including Market Authorization Holders (MAHs) (refer to the definition in glossary) and individuals who have authorized to perform subject matter legally on their behalf.

4.2 Medicine for compassionate use: the responsible person is an authorized person according to Nor.Yor.Mor. 4.

4.3 Narcotics and Medicinal Neuropsychotropic Substances: the responsible person is an authorized person (refer to the definition in glossary) and individuals who have authorized to perform subject matter legally on their behalf.

5. Individual Case Safety Report (ICSR)

5.1 Source of occurrence

5.1.1 Events occurred in Thailand

5.1.2 Events occurred in other countries: the following events should be reported.

(1) Adverse drug reactions in Thai people living in other countries

(2) Adverse drug reactions following product use (approved to be marketed in Thailand), which is sold or is prescribed in Thailand

(3) Adverse drug reactions following product use, which is manufactured in Thailand

5.2 Source of reporting

5.2.1 Unsolicited sources are safety reports after products to be marketed that does not derive from a study or organized data collection scheme, for example

(1) Spontaneous reports

Any relevant data related to adverse drug reaction that occurs in patients after receiving any drug reported by a healthcare professional or consumer

(2) Literature

Any relevant data related to adverse drug reaction that is reported in academic or medical journals as well as published abstracts from conferences. In this case, MAHs only report adverse drug reactions found in academic journal if it could be identified that such drug is known as MAHs' product.

5.2.2 Solicited sources are safety reports after products to be marketed that derive from organized data collection system including research studies, e.g. phase IV clinical study, etc.

5.3 Reporting requirements

5.3.1 Adverse drug reaction According to section 5.1.2, a responsible person should report adverse events occurred either in Thailand or in other countries, and comply with the following (Annex 1)

(1) Serious adverse drug reaction (refer to definition in glossary) any serious adverse drug reaction report from all product types in section 3 must be submitted.

(2) Non-serious adverse drug reaction Only non-serious adverse drug reaction report from the following products should be submitted.

2.1 Vaccines

2.2 New drugs or new biological products with conditional of approval (NC)/(NBC)

2.3 Drugs for compassionate use (Nor.Yor.Mor. 4)

2.4 Other drugs according to Thai FDA announcement

5.3.2 Other drug related problems Any safety issue found should be submitted in accordance with types of adverse events as follow (Annex 1, Flow chart 3)

(1) Resulting in the following serious adverse events

- Lack of effect/therapeutic response decreased
- Pregnancy exposure
- Over dose
- Medication error
- Programmatic error related to vaccines

- Co-incident following vaccination that does not cause by vaccine or programmatic error related to immunization
- Product defect
- Accidental use
- Suicidal attempt
- Drug abuse
- Misuse
- Off-label use
- Occupational exposure

(2) Resulting in the following non-serious adverse events

- Lack of effect/therapeutic response decreased
- Programmatic error related to vaccines

Note 1. Reports should be submitted in compliance with reporting time frame of adverse drug reactions.
2. Definitions are provided in glossary.

5.4 Minimum criteria for reporting

All reports should provide **complete information as much as possible** for the purpose of causality assessment between drugs and adverse drug reaction. The **minimum** information required in submission of adverse event report is:

(1) An identifiable patient

(2) An identifiable reporting source

(3) At least one adverse drug reaction

(4) At least one suspected product

5.5 Reporting timeframe* depends on types of adverse drug reactions as shown below:

Type of adverse event	Period allowed to submit initial report	Period allowed to submit follow-up report
Death	(1) Cause of death from - Vaccines - New drugs or new biological products with conditional of approval (NC)/(NBC) or - Unexpected/unlabeled ADRs Notify Thai FDA immediately, e.g. by fax or e-mail **within 1 business day** after first acknowledgement and submit a complete report within 7 days (2) Other causes Notify Thai FDA within 7 days and submit a complete report within 8 days	Submit a report within 15 days whenever receiving additional information
Serious	Within 15 days	Submit a report within 30 days whenever receiving additional information
Non-serious	Within 2 months	Submit a report within 2 months whenever receiving additional information

*Time frame after MAH's first acknowledgement in Thailand

5.6 How to report adverse drug reaction

Adverse drug reaction can be reported via the following channels

(1) AE-online reporting system which is available at: http://www.fda.moph.go.th/vigilance (prior to access the system, MAH's need to request username and password from HPVC) with or without CIOMS form **or**

(2) Thai FDA adverse event reporting form with or without the CIOMS form by submitting the report via fax, e-mail, mail to HPVC. The forms can be downloaded from the below links:

- Thai FDA adverse event reporting form : http://www.fda.moph.go.th/vigilance

- The CIOMS form : http://www.cioms.ch/index.php/cioms-form-i

5.7 Follow-up report

MAH require to submit the report when they receive additional information, and must clearly specify that is follow-up report along with reference number of initial report. The reporting time frame depends on types of adverse drug reactions as outlined in section 5.5.

6. Other Safety Reports

6.1 Periodic Benefit Risk Evaluation Report (PBRER) or Periodic Safety Update Report (PSUR)

MAHs are not required to submit PBRER or PSUR, unless it is requested by Thai FDA.

6.2 Risk Management Plan (RMP)

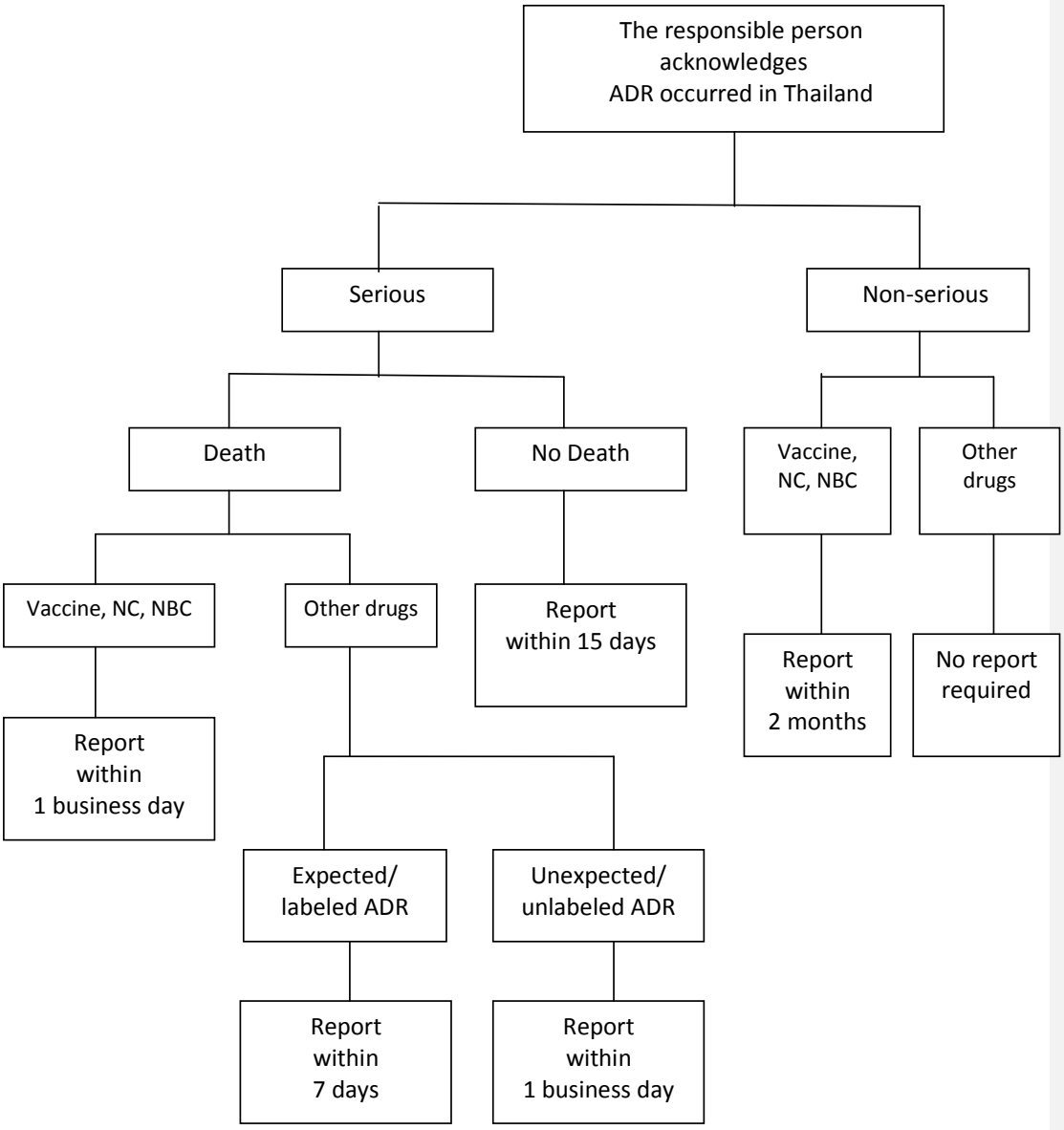
MAHs are not required to submit RMP, unless it is requested by Thai FDA. (refer to RMP template in Annex 4)

6.3 Other Safety Information

In the event that MAHs receive safety information from either research studies or relevant regulatory agency that would effect to the changes of risk management measures, they should submit such information to HPVC, Thai FDA as soon as possible.

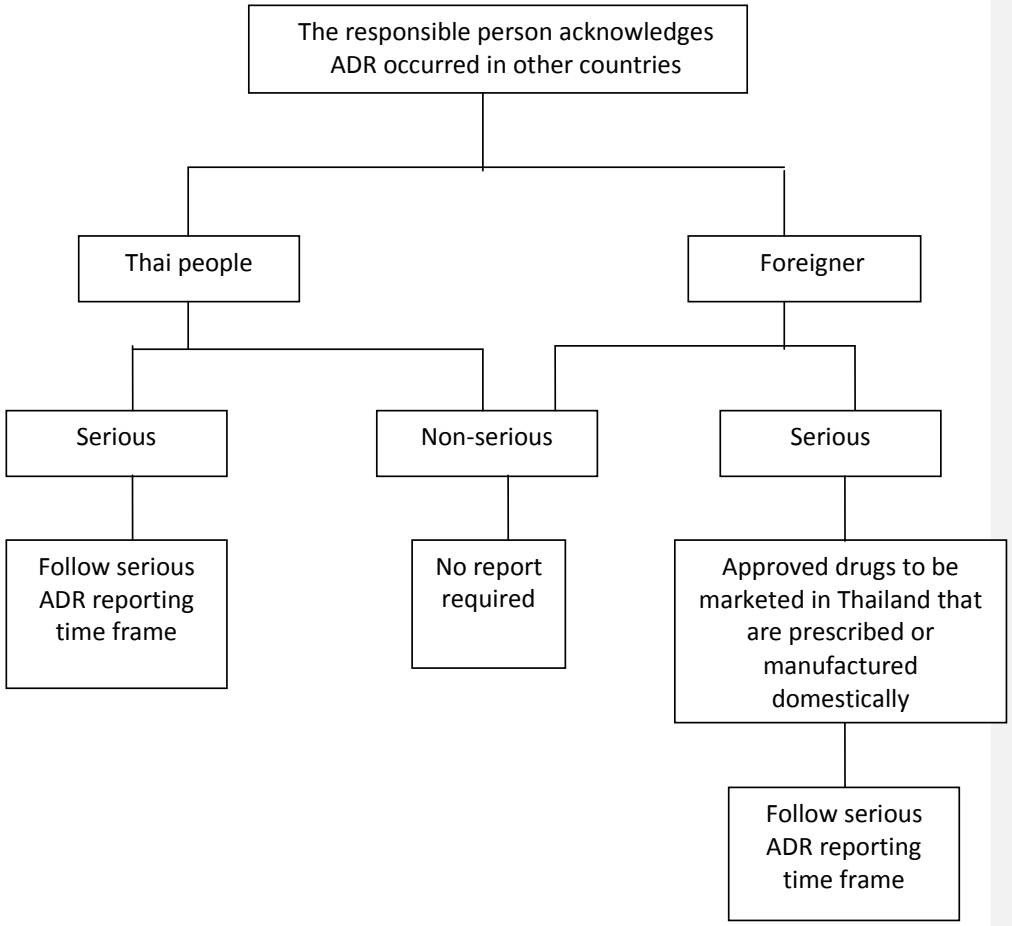
Annex 1

Flow chart 1: Adverse drug reaction reporting occurred in Thailand



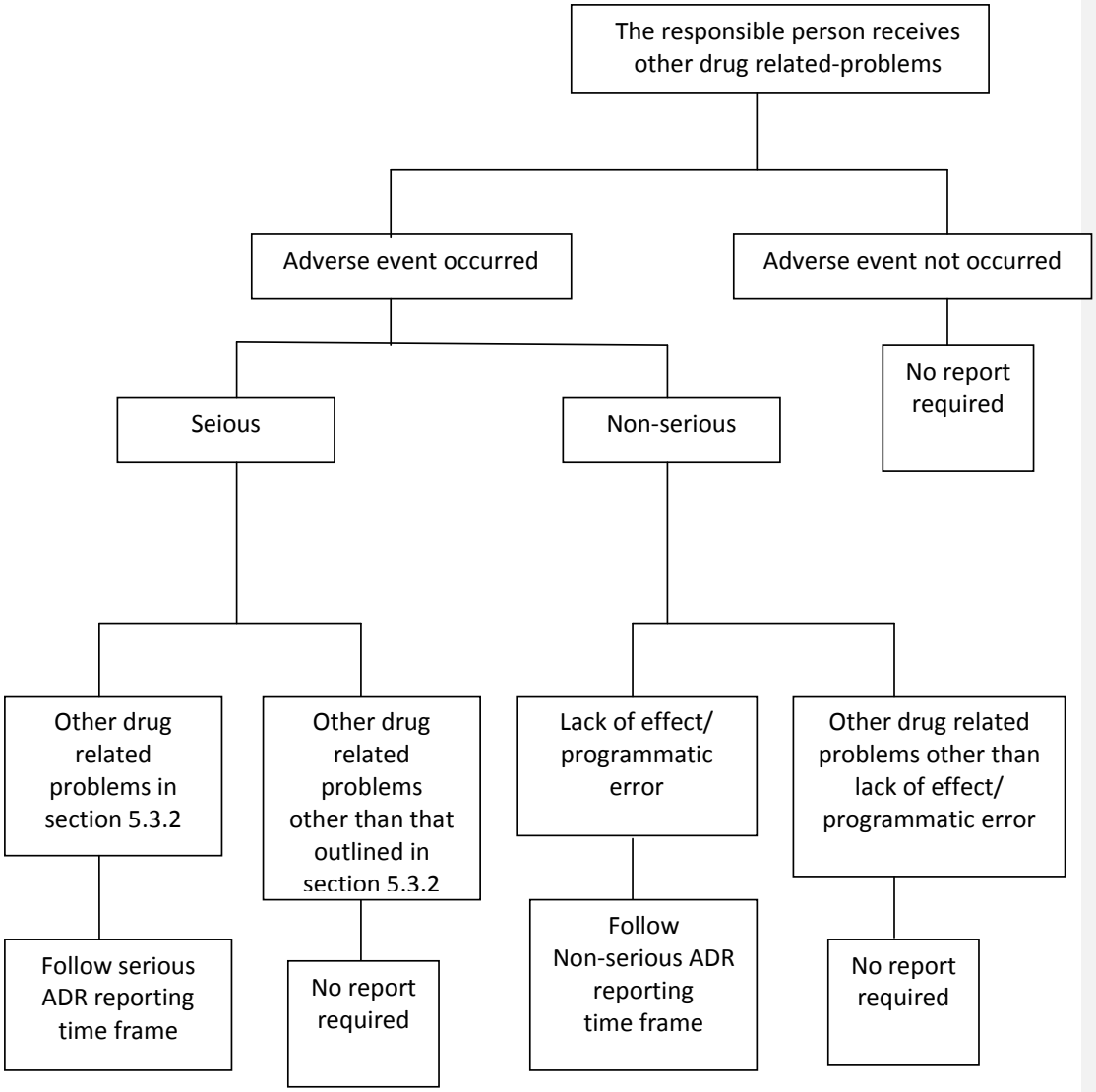
Annex 1

Flow chart 2: Adverse drug reaction reporting occurred in other countries



Annex 1

Flow chart 3: Other drug-related problems reporting



Annex 2

HPVC Form – 1

HPVC No. …… Source/Submitter Report no. ……

Health Products Adverse Event Report Form

❑ Initial
❑ Follow-up no……

(All information will be kept confidential by regulatory authority)

Type of report ❑Spontaneous Reporting ❑Intensive Monitoring ❑ Clinical Trial Reference no……

Patient information

Patient ID ❑ HN…… ❑ AN…… Identification number (13 digits) ……	Type ❑ inpatient ❑ outpatient	Race ❑ Thai ❑ Other (specify) ……	Age	Has allergic history any health product? ❑ No ❑ Yes (specify product name and adverse event)……
Title/Name/Last name	Gender ❑ Male ❑ Female		Weight	Any relevant current disease/condition (please specify ICD code, if applicable) ……

Health Product Information

Type ❑ Medicine/Narcotics ❑ New drugs (SMP) ❑ Food ❑ Cosmetics ❑ Medical device ❑ Hazardous material in public health

Health product (generic/brand name and dosage form; biological-specify batch no. and exp date; herbal medicine – specify proportion used)	S,O I*	Dosage and administration (strength, quantity, frequency, instruction)	Start date D/M/Y	Stop date D/M/Y	Disease or reason for use health product (indicate ICD code, if known)	Health product source (1 or 2)

S=Suspected product, O=Other product, I=Product interaction; Source: 1=Hospital, 2=Others (specify)

Adverse Event Information

Adverse event (describe nature and/or medical term) d/m/y of adverse event……	Labeled or non-labeled (only for ADR)	Laboratory abnormalities and/or physical examination

Seriousness
❑ non-serious
❑ serious (select only one choice)
- ❍ death (specify d/m/y)……
- ❍ life-threatening
- ❍ select only one choice
  - △ requires inpatient hospitalization
  - △ prolongation of existing hospitalization
- ❍ persistent or significant disability/incapacity
- ❍ congenital anomaly/birth defect
- ❍ other medically important conditions (specify)……

❑ Dechallenge
- ❍ definite improvement
- ❍ no improvement
- ❍ unknown

❑ Continue using
- ❍ same dose
- ❍ decrease dose
- ❍ change method of administration

❑ Rechallenge/ Accidentally rechallenge
- ❍ recurrence of symptoms
- ❍ no recurrence
- ❍ unknown

❑ No rechallenge performed

Outcome
❑ Recover without sequelae
❑ Recover with sequelae
❑ Recovering
❑ Not yet recovered
❑ Death (select only one choice)
- ❍ due to adverse reaction
- ❍ health product may be contributory
- ❍ unrelated to health product

❑ unable to follow-up

Reporter information, Source of event, Report location

Name of identifier……
❑ physician ❑pharmacist ❑nurse ❑others (specify)……
Name of evaluator/recorder (reporter)……
❑ physician ❑pharmacist ❑nurse ❑others (specify)……
Report date ……
Source of event location……
Province……Tel……
Report location……
Province……Tel……

Cause of event

❑ Product reaction (ADR/vaccine reaction)
Specify probability level
- ❍ Certain
- ❍ Probable
- ❍ Possible
- ❍ Unlikely
- ❍ Unclassified

(Specify reason)……

❑ Medication error
❑ Programmatic error
❑ Co-incident
❑ Product defect
❑ Accident
❑ Suicide
❑ Misuse/Abuse
❑ Others (specify)……
……

Annex 3

CIOMS FORM

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH			a. AGE	. SEX	4-6 REACTION ONSET			8-12 CHECK ALL
(first, last)		Day	Month	Year	Years		Day	Month	Year	APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING ☐ CONGENITAL ANOMALY ☐ OTHER MEDICALLY IMPORTANT CONDITION

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRO-DUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g. diagnoses, allergies, pregnancy with last menstrual period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER		26-26a. NAME AND ADDRESS OF REPORTER (INCLUDE ZIP CODE)
RIGINAL REPORT NO.	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL ☐ REGULATORY AUTHORITY ☐ OTHER	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP	

Annex 4

Risk Management Plan (RMP)

MAH is responsible to provide risk management plan as requested by Thai FDA. RMP would provide as a part of registration dossier or would submit after a drug is marketed when safety concerns come arise. RMP includes drug safety information, pharmacovigilance plan, and risk minimization measures, with submission to Thai FDA for assessment prior to implementation. RMP preparation procedures and templates are as outlined below:

1. **RMP processes**

1) Determination of safety specification

This step is to identify risk, e.g. ADR occurred in a clinical study, and potential risks, e.g. AE that is caused by pharmacological activity, and that is not found in clinical studies, as well as important missing information, e.g. data from population that does not include in clinical trials.

2) Preparation of pharmacovigilance plan

This step is to assess the major risks mentioned above and to see if additional pharmacovigilance other than routine pharmacovigilance activities, which include the collection of spontaneous AE report, is needed. If additional pharmacovigilance or risk management is required, other activities that could minimize or control risks as described in item 1) should be determined, such as use-results survey, specified results survey, post-marketing clinical study or pharmacoepidermiology study, etc.

3) Preparation of risk minimization plan

The determination of risk minimization or risk control plan as described in item 1) should provide in both routine actions, e.g. risk communication via product package insert, and additional actions, e.g. educational material for prescribers and/or patients, special packaging, establishment of drug usage conditions, and specialized training, etc.

4) RMP review

Periodic RMP monitoring and review should be performed in accordance with new risk information, e.g. addition of risk information in safety specification due to the fact that new adverse reactions is detected from data collection or new information is discovered from investigation or studies. Consequently, pharmacovigilance plan and risk minimization measures would also be updated

in order to conform to new information. This is the preparation cycle of RMP. MAH is responsible to submit all updated RMP to Thai FDA for assessment prior to implementation.

2. RMP structures

RMP must contain the following information and structure:

1) Product general information

1. Generic name of active substance	
2. Brand name	
3. Registration number	
4. Pharmaco-therapeutic group, ATC code	
5. Strength	
6. Dosage form	
7. Dosage and administration	
8. Indication	
9. Date of market authorization	

2) Safety specification

2.1) Non-clinical part of safety specification

(1) Toxicity

Toxicity	**Rationales or evidences to indicate such toxicity**	**Toxicity monitoring activities**	**Activities to minimize or to control such toxicity**
1. Single or repeat-dose toxicity	1. 2.	1. 2.	1. 2.
2. Carcinogenicity	1.	1.	1.

(if applicable)	2.	2.	2.
3. Reproductive and developmental toxicity	1. 2.	1. 2.	1. 2.
Others . . .	. . .	. . .	. . .

(2) General safety pharmacology

General safety pharmacology	**Rationales or evidences to indicate such risk**	**Risk monitoring activities**	**Activities to minimize or to control such risk**
1. Cardiovascular system (QT interval prolongation, arrhythmia)	1. 2.	1. 2.	1. 2.
2.Nervous system	1. 2.	1. 2.	1. 2.
3.Others	1. 2.	1. 2.	1. 2.
. .	. .	. .	. .

(3) Drug interactions

Drug interactions	**Rationales or evidences to indicate such risk**	**Risk monitoring activities**	**Activities to minimize or to control such risk**
1.	1. 2.	1. 2.	1. 2.
2.	1. 2.	1. 2.	1. 2.

3.	1. 2.	1. 2.	1. 2.
.Others .	. .	. .	. .

(4) Other toxicity-related information or data

Other toxicity-related information or data (if applicable)	**Rationales or evidences to indicate such risk**	**Risk monitoring activities**	**Activities to minimize or to control such risk**
1.Antigenicity	1. 2.	1. 2.	1. 2.
2.Immunotoxicity	1. 2.	1. 2.	1. 2.
3.	1. 2.	1. 2.	1. 2.
.Others .	. .	. .	. .

Comment [Meth1]: Unlike the source, this term should be "immunotoxicity" rather than "immunogenicity" , hence "immunogenicity" means "cabable of producign an immnue response", which does not toxicity itself.

2.2) Clinical part of safety specification

(1) Important identified risks

Important identified risks	**Rationales or evidences to indicate such risk**	**Risk monitoring activities**	**Activities to minimize or to control such risk**
1. Adverse events in clinical studies	1. 2.	1. 2.	1. 2.
2. Adverse events from a large quantity of spontaneous reporting	1. 2.	1. 2.	1. 2.
3.	1.	1.	1.

	2.	2.	2.
Others . .	. .	. .	. .

(2) Important potential risks

Important potential risks	**Rationales or evidences to indicate such risk**	**Risk monitoring activities**	**Activities to minimize or to control such risk**
1. Adverse events predicted from pharmacological activities	1. 2.	1. 2.	1. 2.
2. Events observed from drugs in the same therapeutic group and indication	1. 2.	1. 2.	1. 2.
3.	1. 2.	1. 2.	1. 2.
.Others .	. .	. .	. .

(3) Important missing information

Important missing information	**Rationales or evidences to indicate such risk**	**Risk monitoring activities**	**Activities to minimize or to control such risk**
1.Childhood, e.g. neonate, infant, children	1. 2.	1. 2.	1. 2.
2. Elderly	1. 2.	1. 2.	1. 2.
3. Pregnancy or women in lactation	1. 2.	1. 2.	1. 2.

period			
4. Severe liver/kidney disease patient			
.Others .	. .	. .	. .

3) Pharmacovigilance plan

3.1) Routine pharmacovigilance activities including

1. collection of adverse event reports
2.
3.
. .

3.2) Additional pharmacovigilance activities including

1. Use-results survey
2. Post-marketing clinical study
3.Pharmacoepidermiology study
. .

4) Risk minimization plan

4.1) Ongoing risk minimization activities including

1. Provide package insert
2. Provide medication guide to patients
3.

. .

4.2) Additional risk minimization activities including

1. Provide prescribing manual to physician
2. Establish drug usage conditions
3. Restrict only authorized physicians to use the drug
. .

5) Summary of the pharmacovigilance plan

5.1 Ongoing routine pharmacovigilance activities

……

……..

5.2 Additional pharmacovigilance activities

Activity name	**Safety concerns**	**Milestones for evaluation of the activities**	**Action period**	**Status**
1.				
2.				
3.				
. . .				

6) Summary of risk minimization plan

6.1 Routine risk minimization plan

……

……..

6.2 Additional risk minimization plan

Activity name	**Milestones for evaluation of the activities**	**Status**
1.		
2.		
3.		
. . .		

*Structures and processes are applied from "European Medicine Agency, 15 April 2014, EMA/838713/2011 Rev*1 Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 1)" and Pharmaceutical Devices Agency, Japan.*

Annex 5

Glossary

Causality assessment

Causality assessment is the assessment of causal association between a suspected drug and an adverse event.

Lack of effect/therapeutic response decreased; synonym: Ineffective, Failure of expected pharmacological action

Lack of effect is considered an adverse event. The underlying principle is that if a drug fails to produce the expected pharmacological, therapeutic or preventive benefit, there may be an adverse outcome for the patient, including a worsening of the condition for which the medication is being taken.

Pregnancy exposure

Drug used during pregnancy and after pregnancy follow-up with physician is found serious abnormality.

Accidental use

Unintended use or product exposure results in an occurrence of adverse event.

Suicidal attempt

A drug is used intentionally in order that death is the expected result, and may cause adverse events.

Medication error

Any preventable event may lead to inappropriate drug use or patient harm while in the control of healthcare professionals. These events may relate to professional practice, health products, system and working process including prescribing, transcribing, labeling/packaging and naming products, formulation, dispensing, distribution, counseling, monitoring and administration of a drug.

Programmatic error

Any error is caused by storage, shipping, preparation, and vaccination resulting in an adverse drug reaction following immunization. A program error may effect to only single patient or may

lead to a cluster of events associated with immunization. These clusters are usually associated with a particular vaccine provider.

Product defect

Any deviation of the product from its set specification and/or quality; The usage of such product may lead to an adverse event.

Drug abuse

Persistent or sporadic, intentional excessive use of medicinal products which is accompanied by harmful physical or psychological effects.

Drug misuse

Situations where the medicinal product is intentionally used consequence to the occurrence of adverse event.

Off-label use

Situations where a medicinal product is intentionally used for a medical purpose not in accordance with the authorized product information consequence to the occurrence of adverse event.

Occupational exposure

An exposure to medicinal product as a result of one's professional or non-professional occupation results in an adverse event.

Drugs for compassionate use

Drug for compassionate use is the medicinal product with the exception of registration according to the Drug Act including medication to be imported into the Kingdom of Thailand for **charity or donation.** The drug importer must be the authorized manufacturer, the marketing authorization holder, the ministry, the government agency, and the government department responsible for disease prevention and disease therapy, the Thai Red Cross Society, the government pharmaceutical organization, association or juristic foundation, and must submit the Nor.Yor.Mor. 4 application (Drug import permit application for charity or donation) (the announcement of the Ministry of Public Health 14th edition (B.E. 2532) entitled "Requirements, Procedures, and Conditions for Drug Import Permit into Thailand without Pharmaceutical Registration Application") to the Thai FDA.

CIOMS form

An adverse event reporting form developed by the Council for International Organisations of Medical Sciences (CIOMS), intended for notifying the regulatory authorities of countries other than the country where the report originated.

The Authorized Person

Medicinal product (Drug Act B.E. 2510)

The authorized person is a person who is granted a license for manufacturing, importation, or ordering the medicinal product into the Kingdom of Thailand, according to Drug Act B.E. 2510. In case that a license is granted to a legal entity, its manager or authorized representative operating business on its behalf is defined as the authorized person.

Neuropsychotropic Substances

The authorized person is a person who is granted a license according to Neuropsychotopic substances Act B.E. 2518. In case that a license is granted to a legal entity, its manager or authorized representative operating business relating to such substance on its behalf is defined as the authorized person.

Narcotics

The authorized person is a person who is granted a license according to Noxious Narcotics Act B.E. 2522.

Adverse event (AE) or adverse experience

Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Label/unlabeled adverse event

List/non-list of adverse events of approved or registered medicinal product in a particular country

Co-incident

An event occurred accidentally at the same time following immunization is caused by something other than the vaccine product or immunization administrative error, e.g. patient's present illness, complication, etc.

Adverse Drug Reaction (ADR)

A response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function.

An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

For regulatory reporting purposes, if an event is spontaneously reported, even if the relationship is unknown or unstated, it meets the definition of an adverse drug reaction.

Serious Adverse Drug Reaction

A serious adverse drug event/reaction is any untoward medical occurrence which results in

- death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- results in congenital anomaly/birth defect

To ensure no confusion or misunderstanding of the difference between the terms 'serious' and 'severe', the following note of clarification is provided:

The term 'severe' is not synonymous with 'serious'. In the English language, 'severe' is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient /event outcome or action criteria serves as guide for defining regulatory reporting obligations.

Non-Serious Adverse Drug Reaction

A non-serious adverse drug event/reaction is any untoward medical occurrence that **does not result in**

- death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization

- results in persistent or significant disability/incapacity
- results in congenital anomaly/birth defect

Marketing Authorization (MA)

The approval granted by the Thai FDA for marketing in the Kingdom of Thailand.

Marketing Authorization Holder (MAH)

An authorized entity to manufacture or to import the medicinal products into the Kingdom of Thailand

Periodic Benefit Risk Evaluation Report (PBRER)

The periodic review, which covers the significant analysis of new information or benefit-risk related to medicinal product, is used to evaluate the overall benefit-risk of the product.

Periodic Safety Update Report (PSUR)

A systematic review of the global safety data which became available to the manufacturer of a marketed drug during a specific time period, produced in an internationally agreed format.

Risk Management Plan (RMP)

A plan to manage risks associated with the safety profile of medicinal product

Safety Monitoring Plan (SMP)

A specific form of post-marketing adverse event reporting required for new drugs. For at least 2 years after a drug is marketed, it is marked on the label with a triangle within which is written 'must monitor' and the registration number is also labelled 'NC' (new drug with conditions), indicating that all suspected adverse drug reactions associated with the drug should be reported to the Thai FDA according to specific reporting timelines. The distribution of such drugs is limited to hospitals and clinics. In certain circumstances, distribution is limited to only hospitals, and the words "for hospital use only" must appear on the label. At the end of the SMP period, the MAH has to submit a summary of sales, distribution and AE information and comprehensive summary on the safety profile of the new drug which includes domestic adverse drug reaction reports in relation to usage, and safety information from foreign countries, i.e. PSUR, to the Thai FDA. If the safety information is sufficient to demonstrate safety profile of the drug, the Thai FDA may grant an unconditional approval. The drug registration number will be labeled 'N', and the triangle showing monitoring status will be removed. The drug can be available in drugstores if it is classified as a "Dangerous Drug" or "Non-Dangerous Drug" and not a "Special Controlled Drug".

Solicited report

Organized data collection systems, which include clinical trials, registries, post-authorization named-patients use programs, other patient support and disease management programs, surveys of patients or physician or information gathering on efficacy or patient compliance. Solicited reports should not be considered as spontaneous adverse event report**.**

Unsolicited report or Spontaneous report

Any communication by healthcare professionals or consumers to an authorized entity, regulatory authority or other organization (e.g., WHO, Regional Center, Poison Control Center) that describes one or more adverse events in a patient who was given one or more medicinal products and that does not derive from a study or organized data collection scheme.