Notification of Thai Food and Drug Administration

Re: Risk-Based Approach Safety Monitoring Program

As the Thai Food and Drug Administration has set the guide/ bases on safety monitoring program of new drugs after conditional approved for drug registration. According to mentioned conditions for safety monitoring program of new drugs, all new drug categories will be using the same safety monitoring program. However, each new drug category has different risk characteristics, therefore to provide safety protection from post-marketing drug used shall be appropriate and highly effective.

By the virtue of provisions of Clause 6(2) of Ministerial Regulations regarding Drug Registration B.E. 2555 according to the Drug Act B.E.2510, The Thai Food and Drug Administration hereby issue a notification as follows;

(1) To cancel the Thai Food and Drug Administration notification re: Amendment of guide/ bases on safety monitoring program of new drugs dated 6 July B.E. 2555.

(2) Assignation to use Risk-based Approach Safety Monitoring Program according to this notification's attachment.

In this regards, this will be applied to Safety Monitoring Program that has been submitted from 1 January B.E. 2561.

This is announced for acknowledgement.

Notified on Date 9 Month October, B.E 2560

(Signature)

(Dr. Surachoke Tangwiwat)

Deputy Secretary-General acting on behalf of

Secretary-General of the Thai Food and Drug Administration

Attachments

Notification of Thai Food and Drug Administration

Re: Risk-Based Approach Safety Monitoring Program

(Risk-Based Approach SMP)

Content

1. Introduction

New drug that has been registered with conditional approval shall be received Safety Monitoring Program (SMP) which called Intensified (stimulated) reporting. This is the spontaneous reporting safety monitoring with some additional activities in order to stimulate or facilitate the reporting of new product launch into the market. If later, there is sufficient safety information, that new drug will be approved for drug registration without the condition. The purpose is to protect consumer's safety of new drug usage and monitor drug safety effectively. The Thai Food and Drug Administration has created and revised the Guide/ Bases on Safety Monitoring Program of New Drug respectively and issued the latest Thai Food and Drug Administration notification on July B.E. 2555. However, the aforementioned condition of new drug safety monitoring, will be using the same safety monitoring program for all new drugs which they have different risk characteristics, therefore it has been reviewed in order to improve new drug risk-based approach safety monitoring program i.e. high risk drug will be strictly monitored of safety in order to protect the consumer appropriately and highly effective.

As a result, the Food and Drug Administration in association with Pharmaceutical Research and Manufacturers Association (PReMA), Thai Pharmaceutical Manufacturers Association (TPMA) and Regulatory Affairs Pharmacy Association (Thailand) [RAPAT] have revised this safety monitoring program.

2. Objective

To be the regulations for the licensee in order to provide safety monitoring efficiently and maximize the benefits to consumers.

3. Scope

This document will be covered the safety monitoring program of human products as follows;

3.1 New Drugs including new generic drugs which its original has been approved with conditions

3.2 New Biological Products

4. Terminology

Monitored Risk (Watch List) means

Important risk or risk of interest or serious risk that has been found in the process of pre-marketing which must be specified and monitored in the protocol. In the case of protocol amendment, the information shall be revised and informed the Food and Drug Administration, Health Product Vigilance Center in order to disseminate to related persons.

Level 1 Risk Product means

Drug formulations contain incomplete information of clinical research for example; there is no phase 3 clinical research information but it is necessary to use such drug.

Level 2 Risk Product means

(1) Drug formulations' active ingredient is the new chemical entities or new derivatives including complex compounds, Ester or new salt that previously have not yet registered in Thailand.

(2) Drug formulation with new indication

(3) Drug formulation that is the new combination means combination drug that consists of 2 or more new active ingredients and/or registered active ingredients but not duplicate to the registered combination drug.

(4) New Biological Products

Level 3 Risk Product means

(1) Drug formulation with new delivery system where the drug delivery system has been newly developed, provides significantly different in its bioavailability.

(2) Drug formulation with new route of administration

(3) Drug formulation with new dosage form of new registered drug

(4) Drug formulation with new strength of new registered drug

Level 4 Risk Product means Modern drug formulation as follows;

(1) Drug formulation with the same active ingredient as unconditional approved registered drug as follows;

(1.1) Drug that dosage form/ route is

(1.1.1) similar

(1.1.2) different but insignificantly cause a dissimilar adverse drug reaction

(1.2) Strength is

(1.2.1) similar

(1.2.2) different but still in therapeutic dose

(1.3) Indication is

(1.3.1) similar

(1.3.2) new indication but the same daily dose or lesser in the same age group; this will not include biological product which categorized as Level 2 Risk Product

(2) Drug formulation that the manufacturers/ importers/ re-packaged manufacturers has been changed from unconditional approved registered drug (SMP released)

(3) Drug formulation that has been re-packaged from the imported/ manufactured of unconditional approved registered drug (SMP released)

(4) Drug formulation that meets new drug definition registered in overseas more than 10 years and has been globally used with clear evidence that it is safe and effective.

(5) Orphan Drug formulation according to the Thai Food and Drug Administration's notification

(6) Other products that the Thai Food and Drug Administration considered as appropriate for example;

(6.1) Products from human blood and plasma, except the product manufactured by biotechnology unless biotechnology products

(6.2) Antivenom

New Drugs mean modern medicine for human which include

(1) Drug formulation with active ingredient as new chemical entities or new derivatives including complex compounds, Ester or new salt that previously has not been registered in Thailand.

(2) Drug with new indication

(3) Drug formulation that is the new combination means combination drug that consists of 2 or more new active ingredients and/or registered active ingredients but not duplicate to the registered combination drug.

(4) Drug formulation with new delivery system where the drug delivery system has been newly developed, provides significantly different in its bioavailability.

(5) Drug formulation with new route of administration

(6) Drug formulation with new dosage form of new registered drug

(7) Drug formulation with new strength of new registered drug

New Generic Drugs mean modern drug for human which is the new generic drugs including

(1) Modern generic drug formulation for human with active ingredient, strength and dosage from similar to original new drugs in all respects which has been registered since B.E 2534.

(2) New generic drug formulation that its dosage form is different from the original drug formulation, which has already been approved by the committee for the registration of modern drug for human of the new generic drug.

Biological Products mean

Allergens, antigens, vaccines, hormones, cytokines, enzymes, stem cells product, tissues product, human whole blood and plasma derivatives product, immune sera, immunoglobulin, monoclonal antibodies, fermented product or recombinant DNA, diagnostics products directly used with humans or animals or modern drug manufactured from organism by following procedures;

(1) Bacterial culture or eukaryotic cells culture

(2) Extraction of substances from biological tissues including human, animal and plant tissue (allergen)

(3) Recombinant DNA or rDNA techniques

(4) Hybridoma technique

(5) Propagation of microorganisms in embryo or animals, derived from blood and plasma

(6) Other procedure according to minister's notification

New Biological Products mean biological product which is

(1) Biological product formulation that its active ingredient is the new biological active pharmaceutical ingredients, or new derivatives including new complex substances, or new strains which has not yet been registered in Thailand.

(2) Biological product formulation with new indication

(3) Biological product formulation which is the new combination means combination drug that consists of 2 or more new active ingredients and/or registered active ingredients but not duplicate to the registered combination drug.

(4) Biological product formulation with new route of administration

(5) Biological product formulation with new dosage form of the registered new drug

(6) Biological product formulation with new strength of the registered new drug

(7) Biological product formulation manufactured by genetic engineering or other newer biotechnological techniques

(8) Biological product formulation that its active ingredient comes from new source of origin

(9) Biological product formulation that its active ingredient has been changed from inactivated pathogen to live pathogen or live pathogen to inactivated pathogen

Adverse Drug Reaction; ADR means

A response which is unintended and noxious to the body and which occurs at doses normally used in human for prophylaxis, diagnosis, therapy or modification of physiological function Adverse drug reaction does not include the reaction from accidental or intentional drug overdoses as well as drug abuse and misuse of drug. Adverse drug reaction shall present the relationship between the event and the drug for example; by judging that the drug has the least possible relationship to the treatment by reporting or professional healthcare reviewing.

Serious Adverse Drug Reaction; ADR/adverse event; AE means

Reaction/event that led to the following;

(1) Death

(2) Life-threatening

(3) Hospitalization initial/ prolonged

(4) Disability

(5) Congenital Anomaly

Non Serious Adverse Drug Reaction; ADR/ adverse event; AE means

Any other adverse reaction/ event than serious adverse reaction

Spontaneous Reporting means

Report of any adverse reaction/event that professional healthcare or manufacturer found that this adverse reaction/event occur to the patient.

Intensified/Stimulated Reporting means

Spontaneous reporting safety monitoring with some additional activities in order to stimulate or facilitate the reporting of new product launch into the market, the example of this method is safety monitoring program for conditional approved of new drug according to specified timeline.

Mandatory Spontaneous Reporting means

Spontaneous reporting safety monitoring which the licensee shall follow the Thai Food and Drug Administration's notification re: Regulations on Conditional Declaration for Drug Registration of Adverse Drug Reaction Reporting including Vaccine, notified on 5 February B.E. 2559.

5. Regulations on Risk-Based Approach Safety Monitoring Program

Measures of new drug safety monitoring will be depending product risk level which there are 4 levels from the product that contain highest risk will be level 1 to the product that contain lowest risk will be level 4. A level 4 risk product has safety monitoring measures as mandatory spontaneous ADR reporting.

For level 1-3 risk product, they have the guideline as follows;

After the experts/ the committee has reviewed new drug registration application which consist of academic information documents completely and granted the approval with conditions of new drug registration, or after the Thai Food and Drug Administration approved of new drug registration only for the drug that has incomplete information of clinical research but in necessity to use for resolving public health's issues. The licensee shall

5.1 Submit the protocol for drug safety monitoring according to the guideline (Level 1 monitor for all patients (active vigilance), Level 2 and 3 using intensified/ stimulated reporting) including indicate risk that should be monitored (watch list) and revised Thai and English package insert according to the experts/ the committee's resolution to the Bureau of Drug Control, Thai Food and Drug Administration. When the officer has verified the protocol and found it's accurate according to the guideline, the officer will then provide registration number with conditions.

5.2 Represent the message on the label by using triangle symbol on drug label with the text "to be monitored" within the symbol Δ and can be distributed in the hospitals only (both government and private hospitals) with close supervision of the physicians except the drug with extra condition to distribute to the hospitals only.

5.3 Specify contact person for pharmacovigilance who will responsible for coordinating on safety data of post-marketing drug, collecting and safety reporting according to the Thai Food and Drug Administration. Also this person will be able to assess benefit and risk of the drug including provide measures for risk management, qualified with adverse drug reaction reporting training or has basic knowledge of pharmacovigilance and regulations on safety monitoring or qualified with evidences.

5.4 operate according to safety monitoring measures per risk level

5.4.1 Level 1 risk product, monitor for all patients (active vigilance) for example; proactive monitoring such as cohort event monitoring and patient registry

5.4.2 Level 2 and 3 risk product using intensified/ stimulated reporting

5.4.3 Safety Monitoring of Level 1-3 risk product shall be as follows;

(1) Coordinate with the physician, pharmacist or other healthcare professional at the beginning of the drug to be marketed as follows;

(1.1) within 1 month prior to new drug marketed, the important safety information shall be provided such as drug cautions, serious adverse event. The purpose is to promote new drug usage appropriately, fast detect serious ADRs and indicate measures for risk management effectively.

(1.2) after 6 month of new drug marketed, to remind and facilitate of ADR reporting after using the drug to the physician, pharmacist or other healthcare professional (if ADR occurs) every 2 months until 6 months and provide summary operation report within 8 months after the first distribution of new drug.

(2) Following up and safety monitoring by collecting of reports from the physician, pharmacist, professional healthcare and submitting of ADRs report according to the notification of Thai Food and Drug Administration re: Guideline for the licensee to submit of safety reports from post-marketing human drugs, narcotics and psychotropic substances for medical use, notified on 18 December B.E. 2558.

5.5 Submit of reports according to specified timeline and forms (details of form are in the appendix 1) as follows;

5.5.1 During safety monitoring period, please submit

(1) Manufacturing/Packing/Importing or Ordering of New Drug Report each time

(2) 4-Monthly Manufacturing/Packing/Importing or Ordering of New Drug Report

(3) Summary of 4-Monthly Safety Monitoring Results

(4) Summary of Reminders and Facilitations of ADR Reporting

(5) Report of Adverse Event(s) from Healthcare Product Usage

5.5.2 At the end of the safety monitoring period of each product, please submit

(1) New Drug Distribution Report

(2) Data of ADR Reports from hospitals

(3) Presented Adverse Reaction Information

(4) Summary of Amount of Drug Distributed

(5) Summary of Amount of Drug Manufactured/ Re-packed/ Imported or Ordered

(6) Summary of Adverse Drug Reaction from Overseas Usage

(7) Summary of Safety Monitoring Assessment

(8) Comprehensive Summary of Safety Monitoring and Suggestive Measures For Future Safety

Remark: All types of report shall be submitted to the Bureau of Drug Control except case report of adverse event(s) from healthcare product usage shall be submitted to Health Product Vigilance Center.

5.6 Timeline for safety monitoring according to product risk level, since it has been distributed;

5.6.1 Level 1 risk product shall be monitored at least 2 years until there will be sufficient safety information.

5.6.2 Level 2 risk product shall be monitored 2 years.

5.6.3 Level 3 risk product shall be monitored 1 year.

5.7 Submit specified reports within 3 months after the end of safety monitoring period which includes reports of adverse drug reaction from drug used in Thailand compare with the total amount of drug used with information from overseas related to post-marketing drug usage experiences in a number of patients, and specify indicator of safety on drug used appropriately (with safety monitoring measures and reduce the risk of post-marketing drug for example; follow up and report of ADRs, provide/revise of package insert with the current information, provide drug manual for patients) to the Thai Food and Drug Administration. If the reports have not been submitted within the timeline without reasons, Thai Food and Drug Administration may not approve the registration number without conditions or perform other actions as deemed appropriate. After receiving drug registration without conditions, safety monitoring of the drug used will be according to mandatory spontaneous reporting.

Appendix 1: Forms

Ror.Mor.1 Form

Receipt No.....

Date.....

Manufacturing/Packing/Importing or Ordering of New Drug Report each time

[Attached to regulations from the Thai Food and Drug Administration regarding

Procedure on how to perform modern drug registration for human (new drug)

B.E. 2537 dated 31 May B.E. 2537]

Drug Name.....Registration No.....Active Ingredient formulation per unit.....

Name of Organization.....Tel.....Fax.....

Item	Date of Manufacture/ Re-pack/ Import or Order	Lot No. or Batch No.	Amount of drug Manufactured/ Re-packed/ Imported or Ordered	Drug price (per price list)	Location of Drug Storage	Remark

(Signature)..... Licensee

(.....)

(Signature)..... Operating Person

(.....)

Ror.Mor.2 Form

4-Monthly Manufacturing/Packing/Importing or Ordering of New Drug Report

[Attached to regulations from the Thai Food and Drug Administration regarding Procedure on how to perform modern drug registration for human (new drug) B.E. 2537 dated 31 May B.E. 2537]

Receipt No.....

Date.....

Drug Name.....Registration No.....Active Ingredient formulation per unit.....

Name of Organization.....Tel.....Fax.....

Item	Lot No. or Batch No	Amount of Drug Manufactured/ Re-packed/ Imported or Ordered and Drug Price each Month								Total Amount of Drug and Drug Price in 4 Months		Remark
		MM/YY.....		MM/YY.....		MM/YY.....		MM/YY.....				
		Amount of Drug	Price	Amount of Drug	Price	Amount of Drug	Price	Amount of Drug	Price	Amount of Drug	Price	
	Total											

Remark: 1. MM/YY means Month and Year

2. Price means Drug Price per Price List

(Signature)..... Licensee

(.....)

(Signature)..... Operating Person

(.....)

Ror.Mor.3 Form

Receipt No.....

Date.....

New Drug Distribution Report

[Attached to regulations from the Thai Food and Drug Administration regarding Procedure on how to perform modern drug registration for human (new drug) B.E. 2537 dated 31 May B.E. 2537]

Drug Name.....Registration No.....Active Ingredient formulation per unit.....

Name of Organization.....Tel.....Fax.....

Item	Lot No. or Batch No	Name of the Buyer Hospitals	Amount of Drug Manufactured/ Re-packed/ Imported or Ordered and Drug Price each Month								Total Amount of Drug and Drug Price in 4 Months		Remark
			MM/YY..... ..		MM/YY..... ..		MM/YY.....		MM/YY.....				
			Amount of Drug	Price	Amount of Drug	Price	Amount of Drug	Price	Amount of Drug	Price	Amount of Drug	Price	
Total													

Remark: 1. MM/YY means Month and Year

2. Price means Drug Price per Price List

(Signature)..... Licensee

(.....)

(Signature)..... Operating Person

(.....)

Drug Name.....

Registration No.....

Summary of 4-Monthly Safety Monitoring Results

Monitoring Period.....

Summary of ADR Reporting Rate.....

Item	Monitoring Period	Number of patients to be monitored (if applicable) or Amount of drug distributed/ Defined Daily Dose (DDD)	Number of ADR reports	ADR reporting rate	Cumulative ADR reporting rate
	(Month 1st – 4th)				
	(Month 5th- 8th)				
	(Month 9th – 12th)				
	(4-Monthly monitoring until timeline is met according to product category)				
Total					

Remark: DDD information can be found on WHO website http://www.whocc.no/atc_ddd_index/

Drug Name.....

Registration No.....

Summary of Reminders and Facilitations of ADR Reporting

(1 month prior to drug marketed and 6 months post-marketed)

Month/Year	Hospital	Activity(ies) with related documents

Contact Person.....

Tel.....

HPVC No. ..... Report number/Source/Reporter.....

Health Product Adverse Event Report Form

☐ Initial

(All data will be kept confidential of the government)

☐ Follow up .....

Report Type ☐ Spontaneous Reporting ☐ Intensive Monitoring ☐ Clinical Trial Reference No.....

Patient Data

Patient No. ☐ HN..... ☐ AN..... ID No. (13 digits)	Type ☐ Inpatient ☐ Outpatient	Nationality ☐ Thai ☐ Other (specify)	Age	Have the patient had a history of allergy to the product? ☐ No ☐ Yes (Specify product name and adverse event).....
Title/Name/Surname	Sex ☐ Male ☐ Female		Weight	Medical History/ Related patient's other condition (Please specify ICD code, if known).....

Health Product Data

Type ☐ Drug/Narcotics ☐ New drug (SMP) ☐ Food ☐ Medical Device ☐ Hazardous Substances in Public Health

Health Product (Generic Name/ Trade Name, in case of biological product, please specify lot no. and exp. Date, Herbal medicine, please specify the part that has been used)	S, O I*	Dosage and Administration (Strength, Quantity, Frequency unit, Mode of administration	D/M/Y of Start Date	D/M/Y of Stop Date	Disease or Cause of Healthcare Product Using (Specify ICD code, if known)	Healthcare Product Source (1 or 2)

S=Suspected Product, O=Other Product means Other healthcare product that has been used together, I=Product Interaction, Health products that have interaction to each other;

Source: 1=In the Hospital, 2= Others (specify)

Adverse Event Data

Adverse Event Found (Describe the details and/or medical terminology) D/M/Y of event.....	Labeled or Non-labeled (ADR only)	Abnormal Laboratory Result and/or Physical Examination

Serious Level			Results
☐ Non-serious ☐ Serious; (choose only one item) ○ Death (specify D/M/Y)..... ○ Life-threatening ○ Choose only one item Δ Initial Hospitalization Δ Prolonged Hospitalization ○ Disability ○ Congenital Anomaly ○ Other, clinically significant (specify).....	☐ Stop using suspiciuos healthcare product ○ Clearly recovered ○ Not recovered ○ Unknown ☐ Use suspicious healthcare product ○ Use at the same dose ○ Use less dose ○ Change mode of administration	☐ Intentional/ Unintentional Repeat use of healthcare product ○ Same symptom re-occur ○ No symptom re-occur ○ Unknown ☐ No repeat use of healthcare product	☐ Completely recovered without lesion ☐ Recovered with lesion ☐ Improved but not yet recovered ☐ Symptom persisted ☐ Death (Choose only one item) ○ related to Adverse Event ○ might relate to healthcare product ○ Other cause which is not relate to healthcare product (specify) ☐ Unable to follow up

Reporter information, Source of the event and Source of the report	Causation	
Name of person who diagnosed..... As a ☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other (specify)..... Name of Assessor/ Recorder (Reporter)..... As a ☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other (specify)..... Date of report..... Source of the event..... Province.....Tel..... Source of the report..... Province.....Tel.....	☐ Product reaction (ADR/vaccine reaction) Please specify probability level ○ Certain ○ Probable ○ Possible ○ Unlikely ○ Unclassified (Specify reason).....	☐ Medication error ☐ Administration error ☐ coincident ☐ Healthcare product defects ☐ Accident ☐ Committed suicide ☐ Misuse ☐ Other (specify).....

Drug Name.....

Registration No.....

Data of ADR Reports from hospitals

Monitoring period.....

Total ADR reports received.....

Number of hospitals that report ADR.....

Number of ADR reports from Medical School.....

Number of ADR reports from Regional Hospital.....

Number of ADR reports from General Hospital.....

Number of ADR reports from Clinics.....

Date or Period of Report	Hospitals	ADR Report		Remark
		Yes	No	
Total				

Remark: DDD information can be found on WHO website http://www.whocc.no/atc_ddd_index/

Drug Name.....

Registration No.....

Indication.....

Presented Adverse Event Information

Item	Age/Sex	Route of Administration	Daily dose	Duration of use	Time to onset	Reason of drug used	ADR	Labeled/ non-labeled*	Serious level Y= serious N=Non-serious	Result**	Remark

Remark *labeled means ADR that has been indicated in Thai package insert/ non-labeled means ADR that has not indicated in Thai package insert

**Result 1 means completely recovered without lesion 2 means recovered with lesion 3 means Improved but not yet recovered

4 means Symptom persists 5 means death 6 means unable to follow up

Drug Name.....

Registration No.....

Summary of Amount of Drug Distributed

.....

(Data Collection Period)

Item	Hospitals that use the drug	Amount of drug manufactured/ re-packed/ imported or ordered (Please clearly specify unit and packing size)
Total		

Drug Name.....

Registration No.....

Summary of Amount of Drug Manufactured/ Re-packed/ Imported or Ordered

.....

(Data Collection Period)

Date of manufactured/ re-packed/ imported or ordered	Batch No./Lot No.	Amount of drug manufactured/ re-packed/ imported or ordered (Please clearly specify unit and packing size)
Total		

Trade Name.....

Generic Name.....

Summary of Adverse Drug Reaction from Overseas Usage

Report Period.....

Item	Affected Organ System/ Presented ADR	Number of ADR(s)		Remark
		Specified in package insert	Not specify in package insert	
	Total			
	Total			
	Total			
Total				

* Non serious ADR

** Serious ADR

Drug Name.....

Registration No.....

Summary of Safety Monitoring Assessment

Safety Monitoring Period	Number of patients to be monitored (if applicable) or Amount of drug to be marketed/DDD	Number of ADR reports	ADR reporting rate	Remark

Remark: DDD information can be found on WHO website http://www.whocc.no/atc_ddd_index/

Comprehensive Summary of Safety Monitoring and Suggestive Measures For Future Safety

Safety Information for drug registration approval without condition shall contain at least following information

1. Drug name.....
2. Registration No.....
3. Approval date.....
4. Chemical name of active ingredient.....
5. Indication

   .....

   .....
6. Thailand Safety Monitoring Data

   6.1 Number of patient who use the drug (if applicable)

   .....

   .....

   6.2 Amount of drug to be marketed

   .....

   .....

   6.3 Number of reported ADR

   .....

   .....

   6.4 ADR reporting rate in Thailand

   .....

   .....

   .....

   6.5 Symptom and number of serious ADR reported/presented

   .....

   .....

   .....

   .....

6.6 ADR that has not been specified in the package insert (non-labeled ADR)

.....

.....

.....

.....

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7. Overseas Safety Monitoring Data

7.1 ADR that has been specified in the package insert (labeled ADR)

.....

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.....

7.2 ADR that has not been specified in the package insert (non-labeled ADR)

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8. Comprehensive Summary of Safety Monitoring

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9. Suggestive Measures for Future Safety

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Appendix 2

Guidance on Pattern and Procedure Writing (Protocol) of New Drug Safety Monitoring Program

Protocol for new drug safety monitoring program shall at least contain following topics;

1. Objective

To study and monitor new drug safety

2. Procedure

Level 1, 2 and 3 risk product shall be monitored using intensified/stimulated reporting which Level 1 risk product has additional strict procedure of safety monitoring.

Details of safety monitoring program are as follows;

2.1 Level 1, 2 and 3 risk product monitors its safety by providing important safety information (safety issue) / monitored risk (watch list) and facilitates ADR reporting to physician, pharmacist or other healthcare professionals including collects ADR from hospitals all over the country using report form as per requirement and submit the report to Thai Food and Drug Administration periodically as required and within 3 months after the end of safety monitoring period. The company shall summarize, analyze and assess of safety information and submit to related committee for consideration.

2.2 Level 1 risk product has additional safety monitoring in all patients for example; proactive monitoring like cohort event monitoring, interview all patients both pre-treatment and post-treatment in order to collect related information and all types of ADR without changing of study regimen or follow up on patient drug registry

3. Period of time

Monitoring period depends on product risk level since the product has been marketed.

3.1 Level 1 risk product shall be monitored at least 2 years until there will be sufficient safety information.

3.2 Level 2 risk product shall be monitored 2 years.

3.3 Level 3 risk product shall be monitored 1 year.

4. Name of Hospitals

Shall be notified as hospital group such as Government hospitals, private hospitals or clinics, in some cases, this might need to specify agency name depending on types of drug.

If later, there is an additional hospitals other than mentioned above, the Bureau of Drug Control shall be informed within 15 days after the drug has been marketed in such hospital.

5. Reporter

General physician and/or Medical Specialist (specify which specialty area)/ Pharmacist/ Nurse

6. Drug information

Summary table of drug information regarding drug indication, ADR, caution, warning, contraindication and drug interaction from approved package insert shall be provided.

Appendix 3

Guideline on Documentation for Safety Monitoring Program Release Approval

After new drug safety monitoring has been performed according to specified timeline and there is sufficient information to support SMP release, the company shall submit a request for SMP release providing 2 set of information (1 for the Bureau of Drug Control and 1 for the expert reviewer) and rearrange the documents as follows;

1. A letter to Director of the Bureau of Drug Control requesting for SMP release of such drug formulation

- In the case of imported drug for re-packaging, it shall be specified in the letter that the mentioned drug formulation for re-packaging in the country by the licensee use which drug registration formulation (1B), please clearly specify.

2. A copy of Yor.1 form and TorYor.1 form (if applicable)

- If the original drug registration formulation does not specify re-packaged manufacturer or the person who responsible for its release, Yor.1 form shall be attached with complete information and shall be consistent with TorYor.1 form. Please attach supporting documents.

- If the register has been transferred, please attach a copy of previous completed documents.

3. A copy of drug registration certificate

- If there is an endorsement for correction, please copy both sides of document.

4. Latest Thai package insert that has been approved.

5. Latest English package insert that has been approved.

- If there is a revision of package insert, please specify request receipt no. and date of approval.

6. Summary of Amount of Drug Manufactured/ Re-packed/ Imported or Ordered (per required form)

- Specify amount/ packing size clearly for example; blister pack of 10 tablets, contain in a box, 1 blister pack per box, etc.

- In the case of imported drug for re-packaging, please specify packing size of Bulk package and indicate re-packaging information of the corresponding domestic re-packaged manufacturer.

- If the drug has various strengths/ packing sizes, please indicate clearly. Also summarize amount of drug in strengths/ each packing size as appropriate (can be summarized as amount per unit).

7. Summary of Amount of Drug Distributed (per required form)

- In the case of imported drug for re-packaging, which is not for domestic distribution, please use the information from re-packaged product distribution of the domestic re-packaged manufacturer for summary of amount of drug distributed instead.

- If the drug has various strengths/ packing sizes, please indicate clearly. Also summarize amount of drug in strengths/ each packing size as appropriate (can be summarized as amount per unit).

8. Summary of Adverse Drug Reaction from Domestic Usage (per required form)

- In Remark, please specify presented ADR or other remark text, if it needs to be display in this section.

9. Presented adverse reaction information (per required form)

- Please try to understand how to fill accurately and completely in the ADR table.

10. Comprehensive Summary of Safety Monitoring and Suggestion (per required form)

- Provide summary table of all 4-monthly safety monitoring programs and also attach a copy of 4-monthly safety monitoring program of each round that have already been sent.

- Summary of opinions on safety monitoring program, in this part will be the assessment of domestic drug use which should contain following information; Summary of amount of drug manufactured/ re-packed/ imported or ordered/ distributed of the drug in each strength/ packing size, number of patient who use the drug (estimated), categorized presented ADR (serious/non-serious, labeled/ non-labeled), presented number of ADR/ incidence of ADR within the safety monitoring period and provide summary of analyzed of such information including guideline of implementation. Then there might be other information that the person who prepare documents would like to demonstrate additional information. (Such as clinical trial data of drug product that has been studied in Thailand, etc.)

11. Information of overseas drug usage, consists of

11.1 Current drug package leaflet of country of origin

11.2 Periodic Safety Update Report (PSUR) and/or Periodic Benefit-Risk Evaluation (PBRER)

In this part will be data analysis of domestic drug use which has been distributed in that safety monitoring round with current information. In general, Information of PSUR and/or PBRER of at least recent year should be attached.

11.3 Case Reports and/or safety signal

11.4 Summary of Case Reports (per required form)

12. Summary opinions and suggestions on drug SMP released

Summary opinions of safety monitoring which in this part will be data analysis of domestic drug use that has been distributed according to the information in PSUR and/or PBRER with following information; summary of amount of drug distributed for each strength/ packing size, number of patient who use the drug (estimated), categorized presented ADR (serious/non-serious, labeled/ non-labeled), presented number of ADR/ incidence of ADR (only common or serious symptom may be selected, in case of there are a number of ADRs) within the safety monitoring period. And most importantly, if there are serious ADRs or deaths from drug use, information shall be provided and analyzed then summary of analyzed of such information. After that there might be other information that the person who prepare documents would like to demonstrate additional information. And summarize of reason why that registered drug's SMP shall be released.

***Remark**

- If the drug formulation has number of strength and the licensee would like to release the SMP at the same time, please submit the application in the same receipt number.

- Please attach certificate of patent additional information, if there was any change in this part.

- Please attach additional certificate according to notification from the Thai Food and Drug Administration re: Regulations on Conditional Declaration for Drug Registration of Adverse Drug Reaction Reporting including Vaccine, notified on 5 February B.E. 2559.