Asia Partnership Conference of Pharmaceutical Associations (APAC)

Analysis Report

ver. 2014

Identification and Clarification of the Differences in Regulatory Requirements between Asian Economies

APAC Regulations and Approvals Expert Working Group

April 10, 2014
Tokyo, Japan

Member Associations	
HKAP (Hong Kong)	Hong Kong Association of the Pharmaceutical Industry
IPMG (Indonesia)	International Pharmaceutical Manufacturers Group
IRPMA (Taiwan)	International Research-Based Pharmaceutical Manufacturers Association
JPMA (Japan)	Japan Pharmaceutical Manufacturers Association
KPMA (Korea)	Korea Pharmaceutical Manufacturers Association
KRPIA (Korea)	Korean Research-based Pharmaceutical Industry Association
OPPI (India)	Organization of Pharmaceutical Producers of India
PhAMA (Malaysia)	Pharmaceutical Association of Malaysia
PHAP (Philippines)	Pharmaceutical and Healthcare Association of the Philippines
PreMA (Thailand)	Pharmaceutical Research & Manufacturers Association
RDPAC (China)	China Association of Enterprise with Foreign Investment R&D-based Pharmaceutical Association Committee
SAPI (Singapore)	Singapore Association of Pharmaceutical Industries

Abbreviation

Abbreviation	Description
ACTD	ASEAN Common Technical Document
ACTR	ASEAN Common Technical Requirements
ADR	Adverse Drug Reaction
AE	Adverse Event
AIDS	Acquired Immune Deficiency Syndrome
A.O.	Administrative Order (in Philippines)
API	Active Pharmaceutical Ingredient
ASEAN	Association of South-East Asian Nations
BP	British Pharmacopoeia
PBRER	Periodic Benefit Risk Evaluation Report (Philippines)
BSE	Bridging study evaluation
CDCR	Control of Drugs and Cosmetic Regulation (Malaysia)
CDE	Center for Drug Evaluation
CDSCO	Central Drugs Standard Control Organization (in India)
CEP	Certification of Suitability to the monographs of the European Pharmacopoeia
CFDA	China Food and Drug Administration
CFS	Certificate of Free Sale
CIRB	Centralised Institutional Review Board (Singapore)
cGMP	current Good Manufacturing Practice
Ch.P.	Chinese Pharmacopoeia
CMC	Chemistry, Manufacturing and Control
CoA/COA/CA	Certificate Of Analysis
CPP	Certificate of Pharmaceutical Product
CRC	Clinical Research Centre
CRF	Case Report Form
CRO	Contract Research Organization
CSR	Clinical Study Report
CT	Clinical Trial
CTA	Clinical Trial Application
CTA	Clinical Trial Authorization
CTC	Clinical Trial Certificate
CTD	Common Technical Document
CTIL	Clinical Trial Import License(in Malaysia)
CTM	Clinical Trial Material
CTN	Clinical Trial Notification
CTRI	Clinical Trials Registry- India
CTT	Clinical Trial Team
CTX	Clinical Trial Exemption
CV	Curriculum Vitae
DB	Double Blind
DCGI	Drugs Controller General(in India)
DMF	Drug Master File
DOH	Department of Health
DP	Drug Product
DS	Drug Substance
DSRB	National Healthcare Group Domain-Specific Review Board (Singapore)
EC	Ethical/Ethics Committee
EMA	European Medicines Agency
EP	European Pharmacopoeia
EPAR	European Public Assessment Report

Abbreviation	Description
EPW	Empowered Procurement Wing (in India)
EU	European Union
FDA	Food and Drug Administration (in U.S.)
FDC	Fixed Dose Combination
FSC	Free Sale Certificate
FtoF or F2F or FTF	Face to Face
GDA	Generic Drug Application
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GMP CERT	GMP Certification
GpvP	Good Pharmacovigilance Practice
GS-1	Global Standard One
GSB	Global Safety Board
GTIN	Global Trade Item Number
HA	Health Authorities
HAS	Health Sciences in Singapore
HIV	Human Immunodeficiency Virus
HKD	Hong Kong dollar
HSA	Health Sciences Authority (in Singapore)
IB	Investigator's Brochure
IC	Informed Consent
ICF	Informed Consent Form
ICH	The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICH E5	ICH E (Efficacy) 5 Guideline (Ethnic Factors in the Acceptability of Foreign Clinical Data)
ICH E6	ICH E (Efficacy) 6 Guideline (Good Clinical Practice)
ICSR	Individual Case Safety Report
IDL	Import Drug Licence （China)
IEC(EC)	Independent Ethics Committee
IND	Investigational New Drug
IP	Indian Pharmacopoeia
IP	International Pharmacopoeia
IRB	Institutional Review Board
JP	Japanese Pharmacopoeia
KP	Korean Pharmacopoeia
KRW	South Korean won
LOA	Letter of Authorization
MAH	Marketing Authorization Holder
MAV	Major Variation (in ASEAN)
MF	Master File
MFDS	Ministry of Food and Drug Safety
MHLW	Ministry of Health Labour and Welfare（in Japan）
MIDR	Million Indonesian rupiah
MIV	Minor Variation (in ASEAN)
MOH	Ministry of Health (in China)
MOHFW	Ministry of Health and Family Welfare (in India)
MOHW	Ministry of Health, Welfare (in Korea)
MOPH	Ministry of Public Health（in Thailand）
MRCT	Multi-Regional Clinical Trial

Abbreviation	Description
MREC	Medical Research Ethics/Ethical Committee
NADFC	National Agency of Drug and Food Control（in Indonesia）
NBE	New Biological Entities
NCE	New Chemical Entity
NDA	New Drug Application
NDAC	New Drug Advisory Committee
NF	National Formulary
NHG DSRB	National Healthcare Group Domain-Specific Review Board (Singapore）
NIBIO	National Institute of Biomedical Innovation
NiFDS	National Institute of Food and Drug Safety Evaluation
NLT	Not less than
NME	new molecular entity
NPCB	National Pharmaceutical Control Bureau (Malaysia）
NT$	New Taiwan dollar
OTC	Over-The-Counter（drug）
PD	Pharmacodynamics
PFDA	Philippines Food and Drug Administration
PhP	Philippine peso
PI	Principal Investigator
PI	Package Insert
PIC/S	The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PK	Pharmacokinetics
PMDA	Pharmaceuticals and Medical Devices Agency (JAPAN)
PMS	Post-Marketing Surveillance/Study
PP	Philippine Pharmacopoeia
PSUR	Periodic Safety Update Report
r-DNA	recombinant DNA
REMS	Risk Evaluation and Mitigation Strategy
RM	ringgit
RMB	renminbi = CNY (CHINESE YUAN)
RMP	Risk Management Plan
RRC	research review committee
Rs	Rupee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SKU	Stock Keeping Unit
SMF	Site Master File
SMP	Safety Monitoring Program (in Thailand)
SOP	Standard operating procedure
SMPC	summary product characteristics
SQOS	Singapore Quality Overall Summary
SUSAR	Suspected Unexpected Serious Adverse Reaction
TB	Tuberculosis
TFDA	Taiwan Food and Drug Administration
TGA	Therapeutic Goods Administration
TOX	Toxicology
US	United States
USP	United States Pharmacopoeia
WHO	World Health Organization

Survey Results
Data sheets from Each Economy
on the areas of IND, NDA, Clinical Trials and GMP Evaluation System

China	(RDPAC)
Hong Kong	(HKAPI)
India	(OPPI)
Indonesia	(IPMG)
Japan	(JPMA)
Korea	(KPMA)
Korea	(KRPIA)
Malaysia	(PhAMA)
Philippines	(PHAP)
Singapore	(SAPI)
Taiwan	(IRPMA)
Thailand	(PreMA)

Item	Contents	Detail or Example	China RDPAC	Hong Kong HKAPI	India OPPI	Indonesia IPMG	Japan JPMA	Korea KPMA/KRPIA	Malaysia PhAMA	Philippines PHAP	Singapore* SAPI	Taiwan IRPMA	Thailand PReMA
IND	Requirements of the applicant	CRO is possible?	Companies or regulatory agency (CRO)	Basically, CRO and doctors who can follow standards of GCP.	Sponsor companies, CROs and doctors who can follow standards of GCP.	CRO , Companies and doctors who can follow standards of GCP.	Basically, companies and doctors who can follow standards of GCP.	Company, CRO or doctor, who can follow standards of GCP, can be IND holder.	Investigator, or sponsor or CRO can make the application.	Sponsor companies, CROs and doctors who can follow standards of GCP.	Sponsor company should make the application.	CRO can be an applicant (IND holder), just the company registers in Taiwan with legal entity.	Drug manufacturing/import license holder or government (applicant can be sponsor or CRO)
	Clinical trial consultation system	System, Timing, Procedure	There are formal and informal consultations with CDE (Center for Drug Evaluation). 1) CDE started formal consultation system in 2011. 2) pre-IND, IND, end of PhI, end of PhII or pre-NDA are applicable if the product accepted for special review procedure. Flow: application with questions and documents/data (-8Weeks), FtoF meeting, then, fixed minutes (4W) 3) If initiated by CDE, consultation meeting usually is held during IND or NDA review period.	No	Non-formal consultation is possible. Pre-screening of the application is done at DCGI office before accepting our application. 1. IND- For phase 1 trials of NCEs application is referred to IND committee scheduled to meet every quarter(for molecule discovered outside India FIM studies are not permitted. 2. Other IND application -The application is referred to New Drug Advisory Committee (NDAC) for review. Post review, the Sponsor/CRO is invited to a Face to Face meeting with NDAC where they need to present & defend the proposal	The consultation with Head of evaluator is very Tuesday and consultation with Assistant Director of registration every Wednesday or by appointment .	There are many kinds of charged consultation with PMDA. Ex. Pre-PhI/Pre-PhIIa/Pre-PhIIb/End ofPhII study, Pre-application, Quality, Safety, etc. Flow: Tentative application (-8Week), submit the questions and documents (-5W), Inquiries and the answers, PMDA' opinion(<-4day), FtoF meeting, Fixed minutes (30days)	Official pre IND consultation can be held 40 days before expected consultation meeting and it should be requested in written form. Meeting minutes will be issued 10 days after the meeting by MFDS(Ministry of Food and Drug Safety). Pre-review system covers IND preparations. F2F meeting 14~24 days after primary review result.	No	For company-initiated local trial, the proposed clinical trial protocol is prepared by the medical department in consultation with a physician-specialist who becomes a co-author. The protocol is then submitted to the GSB and regional Safety Department & Regulatory Department for approval. The final approval comes from the FDA. For investigator-initiated trials, the proposed protocol is written by the authors subject to the approval of the medical dept of HI-Eisai. The protocol is then sent to the various departments similar to company-initiated trials. (see FDA Circular 2012-007)	No. But for first-in-human trials, HSA would prefer if company has a pre-submission consultation about 2 months before submission.	Regulation consultation service is available for all phases of product development. It is free of charge without legal binding. The way for the consultation can choice official letter response, face to face meeting etc. The procedure should be on-line submission first. Then the project manager of CDE will contact with the applicant for confirm the question which applicant raised and requesting more information. 2 to 4 weeks after the submission will be taken for meeting arrangement. Also the project manager will arrange the appropriate time and attendee list for the consultation meeting. In general, 1 hour for FTF meeting, and meeting minutes may be available 2 weeks after the meeting.	Can consult at FDA (Such as direct contact, telephone)
	Flow of clinical trial notification, IND application and IRB permission	Flowchart	Clinical trial can be initiated after IND approval and IRB permission. In China, clinical trial application is necessary. After getting Clinical Trial Approval (CTA), sponsor should apply for IRB permission with CTA, protocol, IB etc. Even if IRB/IEC review is independent of CTA, all IRB/IEC require CTA as part of the application document.	Approval by DOH is required. IRB approval is also required.	Clinical trial on new drug shall be initiated after authorization by CDSCO (NOC:No Objection Certificate from DCGI) and approval of respective EC. In case of parallel applications, CDCSO will grant conditional approval and note that the trial should start after Ethics approval.	Flow Chart of Clinical Trial Notification see Attachment II a & II b , IIIa & IIIb , IV a & IV b , (See Annex 1)	In Japan, a clinical trial is conducted based on notification, not on application. Contracts with clinical sites should be signed after 30 days from the clinical trial notification (14 days from the second trial onwards).	There is no clinical trial notification system, and only IND approval is available. Clinical trial should be conducted within 2 years after IND approval. (See the flow chart at Annex 2)	Approval by National Medical Research Register is required. IRB approval is also required.	We now have a central ethical review board in the FDA. This board reviews the protocol. Once approved, the CT may proceed. Centers where the clinical trial is to be conducted is notified. Please see FDA Circular 2012-007 (p. 6 &8)	Approval by HSA and IRB approval are required respectively before start of clinical trial. Parallel submissions is possible to both the HSA and the respective IRB.	TFDA has clinical trial notification (CTN) process and general IND application procedure. CTN process only reviews the administration documents by CDE without scientific review for protocol. IRB permission will depend on the site requirement and approval time also depends on IRB. Most contracts with clinical sites need to get IRB approval first prior to sign the contract, the time for contract may take around 2 months.	Apply for IRB or IEC Review and Approval - There are 8 accredited IRB/IEC by Thai FDA - For other study sites that IRB has not accredited, required to submit CT protocol to IRB of MOPH for approval. After IRB/IEC approval, submit the approval letter for IND application Flow chart: Refer to Guideline on Application for Drug Import permit into Thailand for Clinical Trial (2009)
	Time required for clinical trial notification, IND application and IRB permission obtainment	Official timeline: **working days Timeline based on actual experience	IND review usually takes 12+/-2M months at least after application. After IND approval, sponsor should conduct clinical trial within 3 years that CTA is invalid.	3 months	IND review: 6-8 months EC review: 2-4 months	Timeline for evaluation is 14 working days for protocol & amendment of clinical trial after NADFC stated the protocol & amendment complete .	The rule of "after 30 days from the first clinical trial notification" for drugs containing new active ingredients, new ethical combination drugs and drugs with a new administrative route. The clinical trial can be started after 14 days from clinical trial notification for the second trial onwards (for the same product).	IND application official timeline based on the results of the consultation: 30 working days Timeline based on actual experience: Given 1 time query by MFDS during their IND review period, it takes 2-3 months. According to sites, IRB review will be held every 2 weeks to every 2 months depending on the sites. Totally, for initial 3 months, we can get IND approval & IRB approval in parallel.	Official Timeline for CTIL/CTX: for First in Man (FIM), AdvanceTherapy Product (ATP), biological products and herbal products: 45 working days for Others: 30 working days Ethics approval: complete submission without queries can be approved within 4 to 8 weeks.	No specific timelines for trial notification. (Basically not more than 60 days from submission)	HSA review 4-6 weeks (30 days), CTT/IRB review 30-60 days.	The time for CTN will be within 30 days. General IND application procedure will review protocol in detail by CDE and may request to revise protocol based on their review result. the approved time may take around 30 working days. IRB permission time depends. The approve time may takes around 3 to 4 months average.	IND notification : (to Thai FDA) - 20 days IND : (to Thai FDA) - 2 months IRB : (each study site or EC of MOPH) - 4-6 months
IND appli-cation materi als	Application form	Requirements and language	Yes application form (in Chinese)	Application form for Certificate for Clinical Trial	Yes (Form 44, in English)	There is a checklist requirement .	Yes: Clinical trial notification form (in Japanese)	Yes: Clinical Plan Approval Request form (in Korean)	Application form for CTIL/CTX (Clinical Trial Import Licence/ Clinical Trial Exemption). In English or Bahasa Malaysia	Yes, in English. Please see FDA Circular 2012-007	Application form for Clinical Trial Certificate (CTC) to HSA. IRB has no form.	Application form is needed and it can be in English. But the format is in Chinese.	Local form (in Thai)
	A statement regarding the reason why the sponsoring of the proposed clinical trial is	Requirements and language	Yes (in Chinese)	No	Yes (in English) and vernacular language	Yes	Yes (in Japanese)	Yes (in Korean)	No	Please see FDA Circular 2012-007 (p.4)	No	Yes, the official letter to indicate the sponsoring of proposed clinical trial is needed.	Cover letter (have template in Thai)
	Protocol	Requirements and language	Yes (in Chinese)	Yes, in English	Yes (in English)	Yes	Yes (in Japanese)	Yes (in Korean)	Yes, in English or Bahasa Malaysia	Yes, in English	Yes, in English	Required. Chinese or English is acceptable. But for global clinical trial, English version protocol is best choice.	See detail in guideline, can be in Thai or English

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IND appli-cation materi als	IB	Requirements and language	Yes (in Chinese) Usually synopsis or abstract of each report in Chinese is required, attached with source report.	Yes, in English For Ph IV trials, HK registered pack insert can be used.	Yes (in English)	Yes, (in Indonesian or English)	Yes (in Japanese)	Yes (English acceptable)	Yes,in English or Bahasa Malaysia	Yes, in English	Yes, in English	Required. Chinese or English is acceptable. But for global clinical trial, English version is best choice.	See detail in guideline (for unregistered drug in Thailand)
	CRF (sample)	Requirements and language	MRCT: Yes (in Chinese) Import product: No	Yes, in English	Yes (in English)	Yes, (in Indonesian or English)	No, if the description of CRF is to be read by PC.	Yes (English acceptable)	Yes, in English or Bahasa Malaysia	Yes, in English	Yes, in English	Required. Chinese or English is acceptable. But for global clinical trial, English version is best choice.	No requirement
	Informed consent	Requirements and language	MRCT: Yes (in Chinese) Import product: No	Yes, in English or Chinese	Yes- ENGLISH to be submitted to DCGI. ICF in local regional languages has to be submitted to Ethics committee for EC approval. (in a language that is non-technical and understandable by the study subject.)	Yes, (in Indonesian or English)	Yes (in Japanese)	Yes (in Korean)	Yes, in English or Bahasa Malaysia	Yes, in English	Yes, in English	Required. Should be in traditional Chinese.	No requirement
	Investigator's CV	Requirements and language	No	CV of PI	Yes (in English)	Yes, (in Indonesian or English)	No	No	GCP certificate for each investigator.	Yes, in English	CV of PI, in English	Required. Chinese or English is acceptable. But for global clinical trial, usually request PI to provide English version CV.	No requirement
	Non-clinical summary	Requirements and language	Yes (in Chinese)	No	Yes (in English)	Yes, (in Indonesian or English)	No	Yes (in Korean)	Investigator's brochure.	Yes, in English	No	Not required.	including in IB
	Non-clinical report	Requirements and language	Yes (in Chinese) Usually synopsis or abstract of each report in Chinese is required, attached with source report.	No	Yes (in English)	Yes, (in Indonesian or English)	No	Yes (English acceptable)	Investigator's brochure.	Yes, in English	No	Not required.	including in IB
	Clinical summary	Requirements and language	Yes (in Chinese)	No	Yes (in English)	Yes, (in Indonesian or English)	No	Yes (in Korean)	No	Yes, in English	No	Not required.	including in IB
	Clinical report	Requirements and language	Yes (in Chinese) Usually synopsis or abstract of each report in Chinese is required, attached with source report.	No	Yes (in English)	Yes, (in Indonesian or English)	No	Yes (English acceptable)	Published clinical data.	Yes, in English	No (for HSA, every 6 monthly, status report of the trial to be submitted; for IRB usually annually)	Not required.	including in IB
	CMC summary	Requirements and language	Yes (in Chinese)	No	Yes (in English)	Yes, (in Indonesian or English)	No	Yes (in Korean)	Yes	Yes, in English	No	Required. English version is acceptable.	See detail in guideline (for NCE)
	CMC report	Requirements and language	Yes (in Chinese)	No	Yes (in English)	Yes, (in Indonesian or English)	No	Yes (English acceptable)	Yes	Yes, in English	No	Not required.	See detail in guideline (for NCE)
	GMP certificate of the investigational drug	Necessary or Unnecessary	GMP certificate is not required. But a statement that investigational products are formulated in accordance with GMP should be submitted.	Yes	YES.	Yes, (in Indonesian or English)	No	Necessary(This is now under the revision)	Yes	Yes, in English	No (HSA application, to provide GMP certificate of the Drug Product site of Investigation drug, during CTC application)	Yes, provide CoA	unnecessary
	Sample of the investigational drug (for IND review)	Requirements and language	Yes for import product registration.	Yes, proposed label and COA also.	Samples of reference standards and finished product (equivalent of 50 clinical doses or more, if requested by the Authority), with testing Protocol/s, full impurity profile and release specifications. DCGI normaly asks the applicant to submit the samples of the drug product along with reference standard to the government laboratory (Central Drug Testing Laboratory or Indian Pharmacopoeial commission Laboratory). The Applicant needs to submit the samples in the quantity sufficient for three fold analysis.	No	No	No	No, COA only.	Yes (Laboratory testing may be requested)	No	Not required.	No requirement

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NDA	Acceptance of CTD format	CTD or ACTD or Others ?	CTD of CMC for chemical drug with registration category 3~6 can be acceptable. CTD of non-clinical, clinical documents are not acceptable at this moment. CTD of biologicals are still not acceptable.	Not specified. CTD can be accepted.	ICH-CTD is acceptable. However, it is not indicated in document issued by HA.	ACTD format .	Application data for new drugs have to be handled by the CTD format.	CTD format is required for NCE	All applications are made in ASEAN CTD format.	Application data for new drugs have to be handled by the ASEAN CTD format. There is flexibility on the use of ICH dossier as per FDA Adoption of ACTD.	ACTD or CTD	Application for NCE have to be submitted in CTD format.	ACTD
	Category of NDA	ex. NCE, Generic, Supplemental,	1) New chemical entity never marketed in any country. i. Drug substance and its preparations made by synthesis or semi-synthesis. ii. Chemical monomer (including drug substance and preparation) extracted from natural sources or by fermentation. iii. Optical isomer (including drug substance and preparation) obtained by chiral separation or synthesis. iv. Drug with fewer components derived from marketed multi-component drug. v. New combination products. vi. A preparation already marketed in China but with a newly added indication not yet approved in any country. 2) Drug preparation with changed administration route and not marketed in any country 3) Drug marketed ex-China, including: i. Drug substance and its preparations, and / or with changed dose form, but no change of administration route. ii. Combination preparations, and / or with changed dose form, but no change of administration route. iii. Preparations with changed administration route and marketed ex-China. iv. A preparation already marketed in China but with a newly added indication approved ex-China. 4) Drug substance and its preparation with changed acid or alkaline radicals (or metallic elements), but without any pharmacological change, and the original drug entity already approved in China. 5) Drug preparation with changed dose form, but no change of administration route, and the original preparation already approved in China, 6) Drug substance or preparation following national standard. (Supplemental application is also described by regulations.)	Two categories: 1. New Chemical Entity (NCE); 2. Generic (i.e. drug substance already registered at Department of Health (DOH))	New Drug: 1) New Chemical Entity (NCE), 2) New indications, dosage, dosage form and route of administration 3) Fixed Dose Combination (FDC) (See 122E of the Drugs and Cosmetics Rule) Note: all vaccines and Recombinant DNA (r-DNA) derived drugs shall be new drugs unless certified otherwise by the Licensing Authority	A. New Registration , consist of : a. Category 1: New Drug and Biological Product registration including Similar Biological Product / Similar Biortherapeutic product . b. Category 2: copy drug / generic product. c. Category 3: Registration of other preparationt containing. B. Registration of drug variation, consist of : a. Category 4: Major variation registration (VaMa) b. Category 5 : Minor variation registration that needs an approval (VaMi-B) c Category 6.: Minor variation registration with notification (VaMa-A) C. Re-registration : a. Re-registration / renewal .	(1) Drugs containing new active ingredients (2) New ethical combination drugs (3) Druds with a new administration route (4) Drugs with a new indication (5) New dosage form drugs (6) New dosage drugs (7) Follow-on biologics (8) Drugs supplied in an additional dosage form (9) Similar ethical combination drugs (10) Other drugs (Minor changes in approved matters are handled by simply submitting notices.)	<Chemical> (1) Drug containing new active ingredient. 1) New chemical structure 2) Combination drug including novel ingredient (2) Data requering drug(Drug for data-based re-evaluation) 1) Drug with new salt or isomer 2) Drug with a new indication 3) New dosage drug - Increase/Decrease amount of API - New combination drug 4) Drug with a new adminstration route 5) Drug with a new dosage and administration 6) Yeast, Fungi derivated drug : New origines 7) Drug with a new formulation(same route) <Biologics> (3) Drug containing new molecular entities 1) DNA recombinant durg and Cell culture drug 2) Biologics -Vaccine, antitoxins -Blood products -Biologics other than above (therapeutic antigens, botilinium products, ect). (4) Data requiring drug(Drug for data-based re-evaluation) 1) Biologics : strains and manufacturing methods are different from authorized biologics 2) Recombinant DNA products: hosts, vectors, or methods to obtain DNA is different from authorized biologics 3) Cell culture derived products: same cell line, but different cell culture or purification methods from authorized biologics 4) Cell culture derived product: cell line is different from authorized biologics 5) When final bulk is the same, but the site for manufacture is different 6) New dosage forms with the same route of administration 7) Biosimilar product(recombinat DNA) 8) Others not separately classified	1) New Drug Product (New Chemical Entity): any pharmaceutical products that have not been previously registered -New Chemical Entity (NCE)/ Radiopharmaceutical Substance -New Combination Product -Supplemental Product 2) Biologics : - Any products that is produced using biotechnology, this includes vaccines, monoclonal antibodies, blood products, biosimilars, recombinant proteins, etc. 3) Generic product (a product that is essentially similar to a currently registered product in Malaysia. However, the term generic is not applicable to Biologics.)	(1) Drugs containing new active ingredients (2) New ethical combination drugs (3) Drugs with a new administration route (4) Drugs with a new indication (5) New dosage form drugs (6) New dosage drugs (7) Follow-on biologics (8) Drugs supplied in an additional dosage form (9) Similar ethical combination drugs (10) Other drugs Minor changes in approved matters are handled submitting notices and sometimes requires prior approval	NDA-1 for the first strength of NCE. NDA-2 for new combination, new dosage form, new route of administration or new indication of registered chemical entities. NDA-3 for subsequent strengths of a new drug product. GDA-1 for the first strength of a generic chemical product. GDA-2 for subsequent strenths of the generic chemical product.	New Drug I : (1) New chemical entity (2) New indication (3) New combination (4) New administration route New Drug 2 (1) New dosage form (2) New usage dose (3) New unit dose	1) Chemical drugs 1.1) New Drugs (NCE, NI, NCO, ND, NR, NDOS, NS) 1.2) New Generic (NG) 1.3) Generic (G) 2) Biological Products *NCE = New Chemical Entity, NI = New Indication, NCO = New Combination, ND = New Delivery system, NR = New Route of administration, NDOS = New Dosage form of Approved New Drug, NS = New Strength of Approved New Drug

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NDA	Requirement of CPP	Timing of submission. ex. at NDA, before approval Number of required CPP. Source country. ex. Manufacturing/exporting country, Marketing country (FSC)	Import drug require CPP at NDA. Both CPP granted by manufacturing country or marketing country are acceptable.	To be submitted at the time of application No. of CPP required: NCE: 2 ICH countries Generic: 1 (source country only)	CPP or Free sale certificate (FSC) issued by country of origin is required at NDA. The CPP and FSC should be notarised and apostilled or legalised by Indian embassy of the country of origin.	Copy CPP is submitted during pre-registration. The original CPP should be present during registration. CPP only required for imported product. The product with one CPP will evaluated with 300 working days . The product with three CPP (one CPP from manufacturing country , two CPP from harmonized country evaluation{ EU} or country which well known good evaluation system { US, TGA, UK } will evaluated with 150 working days. The renewal of import product should attach with latest/new CPP & latest/new GMP certificate.	Not required	Required for Import Drugs Timing : When CPP is not be submitted at NDA, MFDS(Ministry of Food and Drug Safety) requests it as one of supplementary queries. So it should be submitted as supplementary data. Number : One original document Source : Manufacturing country/Marketing country (It could be submitted separately.)	Category 1 & 2: CPP required at time of application; Category 3: CPP required at time of application but not required for locally produced generics; For imported products, the following requirements shall be furnished, either a: i) CPP from the competent authority in the country of origin; OR (Note: In the event a CPP is not available from the country manufacture, e.g. where a product is not licensed for sale in said country because its manufacturer is manufacturing under contract only for product owner from another country, the following alternatives may be considered: GMP Certification/ Manufacturing License for the manufacturer from the relevant competent authority, together with CPP from the country of the product owner; or CPP from country of release, if CPP from the country of the product owner is not available) ii) CFS and GMP from the relevant competent authorities is deemed acceptable by the Authority for health supplements and natural products only. CPP shall be in the format of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce & be issued by the Health Authorities listed in the WHO Certification Scheme (list is available from WHO website: http://www.who.int).	Timing of submission is at NDA. Number of required CPP is 1 from Source country e.g. ex. Manufacturing/exporting country, Marketing country (CPP or FSC/GMP) or any reference country	Submission of CPP is not compulsory and depends on type of submission. In case of NDA with CPP, basically required at NDA.	At the time of filing, NDA can be submitted without CPP. When approaching approval time, if Taiwan participated two global clinical trials (Ph1+Ph3 or Ph2+ Ph3), (Clinical development in Taiwan in earlier) then CPP can be waived. NDA can be approved with one CPP in one of 10 advanced countries but also need one clinical trial in Taiwan (Ph1 or Ph2 or Ph3) within limited Taiwan subjects enrolled into the study. Product have to be launched in source country or 10 advanced countries.	NDA: Application fees (the charge fee is amended on March 06, 2013, "Fee-Charging Standards for the Registration of Western Medicines and Medical Devices") 1. Product registration of a new drug which is of new active pharmaceutical ingredient(s): NT600,000. 2. Product registration of a new drug which is of new composition or new administration route: NT50,000. 3. Product registration of a new drug which is of a new dosage form, new strength with new indication, new dose unit, or controlled release dosage form, new strength of the same therapeutic compound(s) and the same administration route: NT35,000. GMP Inspections for Western Medicines: 1. GMP Inspections for domestic pharmaceutical manufacturers which is new establishment, relocation, expansion, resumption of operations, or addition of a new active pharmaceutical ingredient, dosage form, process operation, medicinal product: NT60,000; Additional fee of NT20,000 will be charged whenever there is an additional dosage form, biological drug, or active pharmaceutical ingredient. 2. GMP Inspections for foreign pharmaceutical manufacturers 1. Review of a Plant Master File (PMF) of an foreign pharmaceutical manufacturer: NT60,000; Additional fee of NT20,000 will be charged whenever there is an additional dosage form, biological drug, or active pharmaceutical ingredient.
	Approval can be obtained by utilizing foreign clinical trial data.	Requirement of bridging data/report and global clinical trial data/report. Necessity of PK study in local population.	Global / MRCT clinical data for chemical drugs are acceptable, but Chinese P3 and PK data is indispensable. For biologicals, global / MRCT clinical data is unacceptable at this moment.	The overseas clinical trial data is acceptable. Bridging data are not required.	Clinical data in Indian population is required except few life saving therapeutic categories which is at the discretion of the regulatory agency. However now a days, DCGI has become very strict and insists for local clinical trial data for every new drug.	Overseas clinical trial data is acceptable, as long as it is aligned with ICH and/or WHO guideline. Local regulatory trials is required for new pyschotropics and drug for family planning program /	The overseas clinical trial data is accepted in accordance with ICH E5. The drugs approved by using a bridging strategy or global clinical trial data have increased. But Japanese PK data is indispensable.	Only for New Drugs, bridging data is needed additionally. (See figures at Annex 3)	Overseas clinical trial data is acceptable, as long as it is aligned with ICH and/or WHO guidance, and accepted by the major reference countries. Local regulatory trials are not required.	The overseas clinical trial data is accepted.	Overseas clinical trial data is acceptable	The overseas clinical trial data are accepted in accordance with ICH E5. BSE is mandatory for NCE NDA. Complete clinical data package relevant to the Asian population is required to BSE. Bridging study is generally required when there is ethnic difference. A bridging study is to provide clinical data of pharmacokinetic / pharmacodynamic or clinical data on efficacy, safety, dosage and dose regimen in Taiwan that will allow extrapolation of the foreign clinical data to different populations. Taiwanese PK may be waived through BSE submission. Some time may needs Taiwan PK or PD or dose-response data, it depends on the product. The product with ethical difference may needs Taiwan local PK or PD data to support NDA approval.	Not required

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NDA	Application fees	Fees necessary for applying for approval as for NME drug with full data (Category (1))	Application fees of drugs includes: - registration fee: IND:3,500 RMB (local drug) NDA: 20,000 RMB (local drug) IDL: 45,300 RMB (import drug) - drug quality test: around 50,000 RMB, based on test items - GCP inspection: free charge - GMP inspection: free charge	Application fee: HKD 1100 License fee: HKD 1370 Renewal fee (every 5 years): HKD 575	Application fees: NDA: INR 50000 (include MAA fee) Import License: Rs 1000 and at the rate of Rs.100/- for additional drug. Registration Certificate (for import drug): 1500USD for one manufacturing site or its equivalent in Indian currency and 1000USD for one drug or its equivalent in Indian currency. An additional fee at the rate of one thousand US dollars for each additional drug. Duplicate Registration certificate: three hundred US dollars shall be paid for a duplicate copy of the Registration Certificate, if the original is defaced, damaged or lost. Inspection Fee: The applicant shall be liable for the payment of a fee of five thousand US dollars for expenditure as may be required for inspection or visit of the manufacturing premises or drugs, by the licensing authority Test License:The fee of import licences for test and analysis of a drug has been kept Rs. 100 for a single drug and at the rate of Rs. 50/- for each additional drug	Application fee : Pre-Registration : 1 Million IDR (MIDL) Registration fee for : Category 1 : new product & Biological Product : 30 MIDR, new indication : 20 MIDR Category 2: copy product 7.5 MIDR, copy product with BA/BE data: 12.5 MIDR Category 3 : other product: 7.5 MIDR Category 4: VaMa : 2 MIDR for each dosage form/packaging Category 5: VaMa-B : 2 MIDR for each dosage form/packaging. Category 6: VaMi-A : 1 MIDR for each dosage form/packaging. Category 7: renewal : 5 MIDR For pre-inspection GMP document: 7.5 MIDR. For GMP site inspection: three inspector three day = 90 MIDR	Application fees of drugs containing new active ingredients To Government : 533,800 yen To PMDA for review : 23,788,100 yen for paper-based compliance inspection : 6,747,000yen for GCP inspection : domestic 2,801,000 yen, overseas 3,098,000 yen +Travel expense for GMP inspection : domestic 760,900 yen, overseas 960,200 yen +Travel expense	Application fee (1) Chemical : NCE for review : 3,726,000 KRW (STM review + S&E review + GMP review) (2) Biologics : NME for review : 3,726,000 KRW (STM review + S&E review + GMP review) (3) Biosimilar for review : 1,134,000 KRW (STM review + S&E review + GMP review) for GMP/GCP inspection(around 7,500,000KRW/person(overseas)) : This one is the travel expense for inspectors, so if GMP inspection would be waived, no more fee is needed. cf. Generics: KRW 720,000(BE, CMC, GMP review included)	For NCE and NBEs: - Single ingredient: RM4000 -2 or more active ingredients: RM5000 For Prescription products (generic/line extensions): - Single ingredient: RM2200 - 2 or more active ingredients: RM3000	NCE: 450 USD Initial Registration: 340 USD (1USD= 45 PhP) * above rates are current; however these may change pending implementation of proposed new revised fees.	Screening Fees: Abridged/verification $500 Full dossier: $2,750 Evaluation Fees: NDA-1 & NDA-2 (abridged): $11,000, NDA-3 (abridged): $5,500 NDA-1 & NDA-2 (verification): $16,500 NDA-3 (verification): $5,500 NDA full dossier: $82,500 GDA-1 (abridged): $3,850 GDA-2 (abridged): $2,200 GDA-1 (verification): $10,000 GDA-2 (verification): $5,000	NDA: Application fees (the charge fee is amended on March 06, 2013, "Fee-Charging Standards for the Registration of Western Medicines and Medical Devices") 1. Product registration of a new drug which is of new active pharmaceutical ingredient(s): NT600,000. 2. Product registration of a new drug which is of new composition or new administration route: NT50,000. 3. Product registration of a new drug which is of a new dosage form, new strength with new indication, new dose unit, or controlled release dosage form, new strength of the same therapeutic compound(s) and the same administration route: NT35,000. GMP Inspections for Western Medicines: 1. GMP Inspections for domestic pharmaceutical manufacturers which is new establishment, relocation, expansion, resumption of operations, or addition of a new active pharmaceutical ingredient, dosage form, process operation, medicinal product: NT60,000; Additional fee of NT20,000 will be charged whenever there is an additional dosage form, biological drug, or active pharmaceutical ingredient. 2. GMP Inspections for foreign pharmaceutical manufacturers 1. Review of a Plant Master File (PMF) of an foreign pharmaceutical manufacturer: NT60,000; Additional fee of NT20,000 will be charged whenever there is an additional dosage form, biological drug, or active pharmaceutical ingredient.	Not required 2,000 baht (pay after approval)
	Other requirements				Application for Import License is required after marketing approval and Registration Certificate	Specific country requirement on product labeling on product package, example: generic name, retail price, symbol of prescription drug, imported by .		For the NDA of a new drug, i) Safet & Efficacy ii) Standard and Test Method iii) GMPand iv) DMF reiviws are mandatory		Reference Standard Sample (at least 300 mg) PFDA has adopted ACTD format for NDA submission.	For GDA, the reference product must be the registered product with Singapore HSA	NA	
NDA appl-ication materials (NME)	CMC summary	Requirements and language	Yes (Chinese)	for NCE only (document in English)	Yes, in English	Yes (in Indonesian or English as in part II Quality)	Yes (in Japanese as M2 in CTD)	Yes (M2 in CTD, Korean)	Yes (Part 2 in ACTD) - in English or Bahasa Malaysia	Yes, in English	Yes (in English) Singapore Quality Overall Summary(SQOS) is	Yes (In English as M2 in CTD)	Requirement, see ACTD of new drug registration part II / Eng
	CMC report/body of data	Requirements and language	Yes (Chinese)	for NCE only (document in English)	Yes (English is acceptable as M3 in CTD)	Yes (in Indonesian or English as in part II Quality)	Yes (English is acceptable as M3 in CTD)	Yes (M3 in CTD, English is acceptable, but spec.and test methods in Application package should be prepared in Korean)	Yes - in full (Part 2 in ACTD) - in English or Bahasa Malaysia	Yes, in English	Yes (in English)	Yes (In English as M3 in CTD)	Requirement, see ACTD of new drug registration part II / Eng
	Non-clinical summary	Requirements and language	Yes (Chinese)	for NCE only (document in English)	Yes, in English	Yes (in Indonesian or English as in part II Quality)	Yes (in Japanese as M2 in CTD)	Yes (M2 in CTD, Korean)	Yes (Part 3 in ACTD) - in English or Bahasa Malaysia	Yes, in English	Only for full dossier, in English	Yes (In English as M2 in CTD)	Requirement, see ACTD of new drug registration part III / Eng
	Non-clinical report	Requirements and language	Yes (Chinese) Usually synopsis or abstract of each report in Chinese is required, attached with source report.	for NCE only (document in English)	Yes (English is acceptable as M4 in CTD)	Yes (in Indonesian or English as in part III Non Clinical Data)	Yes (English is acceptable as M4 in CTD)	Yes (M4 in CTD, English is acceptable)	Yes (Part 3 in ACTD) - in English or Bahasa Malaysia	Yes, in English	Only for full dossier, in English	Yes. (In English as M4 in CTD)	Requirement, see ACTD of new drug registration part III / Eng
	Clinical summary	Requirements and language	Yes (Chinese)	for NCE only (document in English)	Yes, in English	Yes (in Indonesian or English as in part IV Clinical Data))	Yes (in Japanese as M2 in CTD)	Yes (M2 in CTD, Korean)	Yes (Part 4 in ACTD) - in English or Bahasa Malaysia	Yes, in English	Yes (in English)	Yes. (In English as M2 in CTD)	Requirement, see ACTD of new drug registration part IV / Eng
	Clinical report	Requirements and language	Yes (Chinese) Usually synopsis or abstract of each report in Chinese is required, attached with source report.	for NCE only (document in English)	Yes (English is acceptable as M5 in CTD)	Yes (in Indonesian or English as in part IV Clinical Data). Indonesia required full clinical study report	Yes (English is acceptable as M5 in CTD)	Yes (M5 in CTD, English is acceptable)	Yes (Part 4 in ACTD) - in English or Bahasa Malaysia	Yes, in English	Yes (in English)	Yes. (In English as M5 in CTD)	Requirement, see ACTD of new drug registration part IV / Eng

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NDA appl-ication materi als （NM E）	Other required documents	Requirements and language	application form summary part of application dossiers: (1) Name of the drug (2) Certified Documents, including CPP etc. (3) Objectives and basis for development (4) Summary of CMC, Non-clinical and clinical (5) packaging insert and its reasons, and latest references (6) artwork and labeling	Needs to be in English. General requirement for product registration: 1. Authorization letter from manufacturer – to authorize HKOP register, import and market the product 2. Manufacturer license – original 3. CPP- original 4. Information on the manufacturing facilities and practices of the manufacturer & GMP Certificate - original 5. Registration sample – color photos/scanned image to show the product and sales pack/container appearance. 6. Proposed sales pack – color prototype 7. Proposed pack insert - prototype - The following document(s) to support the proposed indication(s), dosage, route of administration and other contents of the package insert (if any): a. a copy of reputable reference b. documentary evidence showing that the package insert has been approved by one of the listed countries 8. Master formula (Batch formula not accepted) - Non-proprietary names of ingredients, colour Index number or E-number for all colourants used should be provided 9. Finished product specifications 10. Method of analysis 11. COA of a representative batch 12. Stability data 13. Bioequivalence data for anti-epileptic drugs The BE studies should be conducted in accordance with World Health Organization guidance on the "Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability" or other international guideline. 14. Safety documents for ingredients with animal origins Additional requirements for NCE registration 1. 2 ICH country approvals 2. expert evaluation reports on the safety, efficacy and quality of the product. CV of experts who draft the report. 3. EU-RMP and/or US-REMS, if applicable. Information on whether any risk management plan activities and mitigation strategies will be implemented in HK. 4. clinical and scientific documentation substantiating the safety and efficacy of the product.	AS described in Schedule Y of the Drugs and Cosmetics Rules 1945 1.1 Comprehensive table of contents (Modules 1 to 5) 1.2 Administrative information 1.2.1 Application in Form 44 and Treasury Challan (fee) 1.2.2 Legal and statutory documents 1.2.3 Coordinates related to the application 1.2.4 General information on drug product 1.2.5 Summary protocol of batch production and control 1.2.6 List of countries where MA or import permission for the said drug product is pending and the date of pendency. 1.2.7 List of countries where the drug product has been licensed and summary of approval conditions. 1.2.8 List of countries where the drug product is patented 1.2.9 Domestic price of the drug followed in the countries of origin in INR 1.2.10 A brief profile of the manufacturer's research activity 1.2.11 A brief profile of the manufacturer's business activity in domestic as well as global market. 1.2.12 Information about the expert(s)/ Information regarding involvement of experts, if any 1.2.13 Environmental risk assessment 1.2.14 Samples of drug product	ACTD Section I : Administrative Doc.& Drug Information (SMPC & Patient Information Leaflet) Sub Section A: All Table of Content Sub Section B: Administrative Documents ☐ Registration Form ☐ Statement of Applicant ☐ Certificate and other Administrative Documents ☐ Result of Pre-registration ☐ Invoice/ Receipt of paymen & other documents Sub Section C: Product Information and Labeling Section II: Quality Documents Sub section A: Summary of Quality Document Sub section B: Quality Documents S. Active Substance P. Finished Drug Section III : Non clinical Study Section A: Review of Nonclinical Study Section B: Summary and PreClinical Study Matrix Section C: Non Clinical Study Report x Section D: References Section If the manufactured not yet registered, it should provide SMF.	CTD Part I (Module 1) 1.1 Table of Contents 1.2 Approval application (copy) 1.3 Various certificates 1.4 Information on patent matters 1.5 Data concerning the origin or background of development 1.6 Information on the use of the drug in foreign countries 1.7 List of similar products from the same therapeutic category with the same efficacy 1.8 Package insert 1.9 Documents pertaining to the non-proprietary name of the drug 1.10 Summary of data pertaining to the designation as a poisonous drug, etc 1.11 Master plan for post-marketing surveillance 1.12 List of attached data 1.13 Other data	Module 1 1.1 Table of contents of Module 1 1.2 Application form or approval application(Copy) 1.3 Signature of the person in charge of preparation of CTD, His/Her information(career) 1.4 Certificate of translator 1.5 Information on the use of the applied drug in foreign countries 1.6 Information on comparison with other similar products available in the Korean market and properties of the applied drug 1.7 Various documents related to Enforcement regulation of Pharmaceutical Affairs Act Article 24-1) 1.7.1 Bioequivalence test data/ Dissolution test data 1.7.2 CPP 1.7.3 GMP data 1.7.4 DMF data 1.8 A contract(In case any process during manufacturing, QC test would be outsourced) 1.9 LTOC 1.10 Package insert(draft) 1.11 Other data	In English or Bahasa Malaysia: ACTD Part I :Administrative Data And Product Information Section A: Product Particulars Section B: Product Formula Section C: Particulars Of Packing Section D: Label (Mockup) For Immediate Container, Outer Carton And Proposed Package Insert Other admin doc: CPP, LOA, CA, GMP CERT	Please refer to ACTD list of requirement	Module 1 (or ACTD Part Ⅰ) documents e.g, Letter of authorizations Declarization Artwork of packaging material GMP certificate Patent declaration Reference country/product approval and approved package insert, if applicable	CTD Module 1 (Taiwan Specific) CTD formate was announced in July 2012 and became mendatory for NCE products since Nov. 01, 2012. New Drugs other than NCE, as well as generic products also need to be submitted in CTD format starting from July 01, 2014. 1 Administrative Information and Prescribing Information 1.1 Table of Contents of the Submission Including Module 1 1.2 Application Fee Receipt 1.3 Official Letter and Document 1.4 Application Form (original copy and duplicate copy) 1.5 Affidavit 1.6 Form for Sticking Label and Package Insert 1.7 Certificate/License 1.8 Letter of Authorization 1.9 CPP of Source Country 1.10 Formulation Basis 1.11 Certificate of PIC/S GMP/cGMP 1.12 CPP 1.13 Bridging Study Evaluation 1.14 Status of Clinical Study Taiwan involved 1.15 Status of Bioavailability (BA)/ Bioequivalence (BE) Study Taiwan involved 1.16 Contract Manufacturing 1.17 Applications of Contract Analysis 1.18 Radiation Dosage Study Report 1.19 Risk Evaluation and Mitigation Strategy (REMS) 1.20 Other Documents or Reports	Requirement, see ACTD of new drug registration part I / Eng

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Approval review	Review organization	Review organization, Decision organization, Advice committee	Review CDE (Center for Drug Evaluation) Decision CFDA (China Food & Drug Administration) Inspection Regional Drug Administration	Review: Drug Office, DOH Approval: Pharmacy and Poisons Board	CDCSO/DCGI (Drug Control General of India) Twelve New Drug Advisory Committees (NDAC) were newly constituted to examine the applications for permissions for clinical trials and approvals for new drugs.	1. Committee of Safety-Efficacy Evaluation with the task of evaluating the safety and efficacy aspect to be discussed in the periodic meeting of National Committee/ KOMNAS. 2. National Committee on Drug Evaluation with the task of discussing , formulating, giving consideration and decision of the results of drug evaluation through a periodic forum meeting. 3. Committee of Quality Evaluation with the task of evaluating the quality aspect. 4. Committee of Product Information Labeling Evaluation with the task of evaluating in the aspects of Product Information and Labeling.	Review PMDA (Pharmaceutical and Medical Device Agency) Decision MHLW (Ministry of Health, Labour and Welfare) Advice CDFS (Council on Drug and Food Sanitation)	MFDS and NiFDS(National Institute of Food and Drug Safety Evaluation) Advice : Central Pharmaceutical Affairs Council	National Pharmaceutical Control Bureau (NPCB): Receive and review the new drug applications, and propose it to the Drug Control Authority (DCA) for approval/rejection. Drug Control Authority (DCA): A committee that meets once a month to decide on new product registrations & licenses.	Philippines FDA	HSA (Panel of internal and external reviewers.)	-	Thai FDA
		Number of reviewers ex. Clinical, Non-clinical, CMC, Chemical/Biological	All staffs : 103 Traditional Chinese drug : 16 CMC : 25 Biologics : 8 Non-clinical : 13 Clinical : 20 Biostatistics : 3 Clerical work : 18 (As of August, 2013)	Undisclosed	CDSCO total manpower 327 (as of 2009). No detailed information.		All staffs : 714 (As of Oct 1, 2013) Pharmacology : 384 Medical doctors and Dentists : 42 Engineering : 44 Veterinarian and Toxicity : 25 Biostatistics : 13 Science and agriculture, etc. : 63 Clerical work : 101 (As of April 1, 2012)	MFDS Chemical Administration(Drug policy): 44 GMP: 21 Clinical Trial Management: 18 Narcotics: 15 Bio Administration(Bio policy): 21 Bio GMP: 15 Traditional medicine: 11 NiFDS Drug Review Management: 28 Pharmaceutical Standardization: 15 Circulating System: 17 Oncology: 13 Digestive System: 17 Bioequivalent: 22 Biologics: 19 Recombinant Protein: 16 Cell & Gene Therapy: 13 Herbal: 11 Regional KFDSs	Total NPCB staff: ~ 380 Reviewers in Centre for Product Registration: 80	All staffs : 400 FDA employees	GMP on-site inspection or PMF registration (paper review) is requested and the approval should be got then NDA can be approved accordingly. Otherwise NDA Approval will be held until GMP sttus confirmed (inspection or PMF approval). The GMP compliance check should be done by TFDA for each manufacturing site, even toll manufacture site or packaging site.	Division of Medicinal Products under TFDA, which is responsible for all drug products, has around 100 active staff including administrative, drug safety and regulation build-up. Among the menpower, about 40-50 staff belong to new drug, generic drug and clinical trial reviewing force.	See Attached sheet-Number of reviewers (Annex 8)
	Review process	Append the flow of the review of applications for new drug with the attached paper.	CFDA accepts the NDA application documents and transfer these documents to CDE in 30 work days, then CDE reviews and evaluates it in 150days ,finally, CFDA approves it in 30 work days. CDE review process for IND/NDA is attached for reference.	Undisclosed	DCGI accept the application in Form 44 and then it is forwarded to NDAC for expert review.	Pre-registration review document until complete documents --> Payment of pre-registration fees --->submit pre-registration --> Evaluation--> Approval Pre-Registration Registration review document --> Payment of registration fees --> Submit registration documents --> Clock start of registration review Note : * Only NCE/Biological Product Non-Clinical & Clinical were evaluated through Committee of Safety-Efficacy evaluation and National Committee then continue with Committee of Quality Evaluation , and Committee of Product Information. *Others (Generic & variation) were evaluated with Committee of Quality Evaluation , and Committee of Product Information. .	See Annex 6	See figures at Annex 7	Dossier Submission via online--> Screening & Acceptance of dossier via online --> Payment of registration fees--> clock start of registration review--> Sending for external expert review on clinical section for NCE/Biologics--> Evaluation Committee's recommendation -> Decision by Drug Control Authority. (Annex 4)	Please see Flowchart_PSD_ revised_Aug 2007	Screening/evaluation/queries, input requests/regulatory decision	See Annex 5	Annex 9 - the timeframe for approval

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Approval review	Review time	The standard period of time from acceptance of applications to the approval of new drugs.	Official timeline of CTA / NDA of import drug from submission to approval: 145 working days But, actual timeline is much longer. The recommendation timeline for 2013 by RDPAC: CTA or NDA of import chemical drug is 22 or 23 months; Initial MRCT of category 1 drug is 12 months while MRCT of category 3 drug is 13 months. (MRCT:Muti-Regional Clinical Trial)	NCE: 12-15 months Generic: 9-12 months	About 12-15 months for marketing approval and registration certificate. About 3 months for Import License.	Timeline of pre-registration 4 0 working days after completed documents for category 1,2,3,4,5.Timeline of registration 100 working days after completed documents for : a. New Drug & Biological Product that are indicated for the treatment of serious life-threatening human disease , or classify as Orphan drug, or classify for public health program, or new drug which development by Pharmaceutical industry / research institution in Indonesia b. New registration of generic essential copy drug. c. New registration of copy drug with standard electronically information (Stinel). d.Major variation . Timeline of registration 150 working days after completed documents for a New Drug , Biological Product , major variation with : 3 (three) CPP from countries with known good evaluation, system or approved in the country that has applied harmonized evaluation system (EU , EPAR, EMEA). b. New Registration of Copy Product without Stinel. Time line of registration of 300 working days after completed documents:1 CPP from original country.	Review time of FY 2012(Median) Priority review products : 6.1 months Standard review products : 10.3 months	Practically around 12 months are needed for NDA.	NCE/NBE: 245 Working days Priority review : 6-9 months Generics: 210 working days	Review time of FY 2012 (Median) Priority review products : 9 months Standard review products : 15 months New lead time: 18 months	Screening: 25 working days Evaluation: Full dossier: 270 working days Abridged: 180 working days Verification: 60 working days	Review time Priority review products: 12 months standard review products: 18 months	Annex 9 - the timeframe for approval
Approval review	Priority review system	Presence of priority review system, Content of system, Subject drug for priority review ex. unmet medical needs, for serious life-threatening disease	Special review procedure exists, which is appropriate for following applications of new drugs: 1) Active ingredients extracted from plants, animals or minerals, etc. and their preparations not yet marketed in China, and newly discovered Chinese crude drugs and their preparations; 2) Chemical drug substance and their preparations and biological products not yet approved for marketing in China or abroad; 3) New drugs for the treatment of diseases such as AIDS, malignant tumors and rare diseases, etc. with significant clinical advantages; and 4) New drugs for the treatment of diseases, for which effective therapeutic method is not available. For those drugs specified in items 1) & 2), the applicant of drug registration (hereinafter "the Applicant") may apply for the special examination and approval when submitting the application for clinical trials of the new drugs. For those drugs specified in items 3) & 4), the Applicant may apply for the special examination and approval only when submitting the production applications.	usually no; except official request from Hospital Authority upon urgent situation	There is no formal priority review system. Depends on therapeutic area and unmet requirement.	There is no priority system. The review following the timeline of registration (100 or 150 or 300 working days)	The priority review system exists. Orphan drugs receive priority review automatically. New drugs not designated as orphan drugs which target other serious diseases and which are apparently expected to contribute to the improvement of quality of healthcare may be designated as "non-orphan priority review products" based on overall evaluation of the seriousness of the target disease and medical usefulness of the drugs. Designation is made based on the opinions of external experts if an application is submitted with an application for marketing approval.	The priority review system exists 1) Drugs which target for life-threatening or serious diseases such as AIDS, cancers etc. 2) Drugs of which is deemed necessary because treatment is not possible with existing therapies due to resistance or other reasons 3) Other drugs such as anti-cancer agents, orphan drug, DNA chip etc : recognized by MFDS minister for patients or industrial development 4) Herbal medicines for cancer or AIDS	There is no formal priority review system in place. Priority review status will be provided on case to case basis, based on the applicant's justification. Usually priority review status is granted for the following group of products: - life-saving products, e.g. viral infection/oncology drugs - fulfill unmet medical needs - treatment for rare diseases where currently there isn't a treatment option available.	The priority review system exists. For serious diseases and life-threatening conditions and which are apparently expected to contribute to the improvement of quality of healthcare based on overall evaluation of the seriousness of the target disease and medical usefulness of the drugs. Consideration is made based on the opinions of external experts if an application is submitted with an application for marketing approval.	No separate priority review system or pathway. Only if product is submitted via Abridged Evaluation (with 1 reference country approval); and meets the pre-defined criteria in the guide (unmet medical need, etc). Grant of priority review is on case-by-case basis, at discretion of the Agency during Screening. Applicant will be notified at the point of acceptance of application, if request is granted.	The priority review system exists Unmet medical needs and drug for serious life threatening disease and is major medical advance can apply to priority review system. It should be apply for priority review first, after recognition by TFDA as priority review case then can be reviewed by priority review process. TFDA release new regulation for NCE -2 simple review regulation. For the product which launch in top 10 countries for over 10 yrs, the review process could be simpfy. For the product which approval by both USFDA and EMA, they product could also apply the simple reivew system.	There will be the fast track for life-threatening desease e.g. HIV drug, anti-cancer drug.

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Approval review	Orphan drug system	Presence of orphan drug system, Criteria for designation, Incentive, etc.	No orphan drug designation system.	No	The orphan drug system does not exists.	The orphan drug will evaluate will evaluated within 100 working days. No regulation establishing for Orphan drug.	The orphan drug system exists. Designation criteria <u>Number of patients</u> Less than 50,000 in Japan <u>Medical need</u> There are no appropriate alternative drugs or treatment methods. The efficacy and safety are expected to be outstandingly greater than those of existing drugs. <u>Possibility of development</u> There is a theoretical ground for using the drug for the target desease and the development plan is acceptable. Incentives (1) Subsidy payment(The total budget for financial year 2010 was 650 million yen.) (2) Guidance and consultation on research and development activities (HMLW, PMDA, NIBIO). PMDA provides a priority consultation system. (3) Preferential tax treatment (4) Priority review (5) Extension of re-examination period The re-examination period for the drugs will be extended up to 10 years.	The orphan drug system exists. <u>Designation criteria</u> -Prevalence is less than 20,000 in Korea -Drugs to treat diseases for which appropriate therapy and drugs have not been developed or have been significantly improved in terms of safety and/or efficacy, compared to existing alternative drugs - Pharmaceutical product whose annual sum of importation does not exceed 1.5 million USD or annual sum of GDP does not exceed 1.5 billion KRW(On condition that less than 500 pateints in Korea, pharmaceutical product whose annual sum of importation does not exceed 5 million USD or annual sum of GDP does not exceed 5 billion KRW) - Products which do not meet the criteria above can be designated as an orphan drug if it is acknowledged that the limited supply of product would cause any serious harm to the concerned population or the MFDS minister recognizes it. Incentives 2) Exemption of following data 1) CMC(specification and test method) : No review, but in-house spec. should be submitted 2) GMP 3) DMF 4) following data for S&E review - bridging data - Some Toxicity data : only single dose toxicity and 1 to 3 months repeat dose toxicity data are needed - Pharmacology data will be replaced by pharmacodynamic data or clinical trial data - Phase 2 study will be included in phase 3 study 5) Some regulations on Korean labeling 3) Priority review	The MoH is in the process of establishing the orphan drug system; the industry has been engaged for consultation on a proposed guideline. Meanwhile, the registration of orphan drugs follows the standard/priority review registration track.	The orphan drug system does not exists but we have a DOH A.O. 4 s. 1992 for Compassionate Special Permit for life-saving drugs. This is the closest that we can get in as far guidelines for orphan drugs are concerned.	Available in Regulations but implemented as Named-Patient Basis pathway.	The orphan drug system exists. Designation criteria: <u>Number of patients:</u> the standard for rare diseases is if it's prevalent in less than 1/10,000. It is different with US (U.S. it is considered a rare disease if it affects less than 200,000 people/ prevalent in less than 7.5/10,000) and Japan (the number of patients total less than 50,000 /prevalent in less than 5/10,000) <u>Definition of Rare Disease:</u> The rare diseases specified in this Act refer to diseases with prevalence lower than that formulated and publicly announced by the central competent authority, and recognized by the Committee specified in Article 4 of this Act; or diseases designated and publicly announced by the central competent authority under special circumstances. Reward: To encourage the R&D and manufacturing of orphan drugs, TFDA announced and implemented the "Rewarding Standards for the Manufacturing and R&D of Orphan Drugs. But it focus on Domestic manufacturer.	Available, the requirement for orphan drug registration is only Admin part and some of Quality part.
	approval matters	You may append the approval matters with the attached paper.	・Approval number ・Marketing License Holder and its address ・Manufacturer and its address ・Non-proprietary Name ・Brand name in Chinese if applicable ・Active ingredents and Contents or Nature ・Dosage form ・Dosage strength ・Packaging size ・Shelf life ・Specification & test methods ・labeling and artwork ・packaging insert		・Generic Name ・Brand name ・Manufacturing Method ・Dosage and Administration ・Indications ・Storage Methods and Expiration Date ・Specifications and Test Method ・Name of the Manufacturing Site used to Manufacture the Product	Besides Marketing Authorization , it attached with : * Registration Form * Approved Labelling * Approved Package Insert * Approved Patient Information Leaflet	・Non-proprietary Name ・Brand name ・Ingredients and Contents or Nature ・Manufacturing Method ・Dosage and Administration ・Indications ・Storage Methods and Expiration Date ・Specifications and Test Method ・Name of the Manufacturing Site used to Manufacture the Product, Address, License/Accredetation Category, etc.	・Non-proprietary Name ・Brand name ・Ingredients and Contents or Nature ・Appearance ・Manufacturing Method ・Dosage and Administration ・Indications , Precautions for use ・Storage Conditions and Expiration Date ・Specifications and Test Method ・Name of the Manufacturing Site used to Manufacture the Product, Address, License/Accredetation Category, etc. ・Approval condition, if necessary	A regulatory decision shall be made based on the outcome of the evaluation of the submitted documentation. An application may be approved or rejected by the Authority, and the Authority decision will be sent via email/ official letter to the product registration holder. Upon registration of a product by the Authority, the product registration holder shall be notified by the Authority and a product registration number (i.e. MAL number) shall be assigned to the registered product. Registration status of a product shall be valid for five (5) years or such period as specified in the registration notification (unless the registration is suspended or cancelled by the Authority).				

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Approval review	Other information concerning approval review			N/A		NCE should provide API Drug Master File or Internal Monograph as required in Part II Quality . Approval of SMF should also be considered to get approval of registration number.			As stipulated under the CDCR 1984, Regulation 11(1), the Authority may, at any time reject, as well as cancel or suspend the registration of any product if there are deficiencies in safety, quality or efficacy of the product or failure to comply with conditions of registration. Any person aggrieved by the decision of the Authority or the Director of Pharmaceutical Services, a written appeal may be made to the Minister of Health Malaysia. All notice of appeals shall be made within fourteen (14) days from the date of notification from the Authority. A period of 180 days from the date of notice of appeal is given for submission of any additional information/ supplementary data/ documents for New Drug Products and Biologics. A period of 90 days is allowed for other categories of product. Re-submission for product registration of a rejected application due to reason of safety and efficacy shall not be accepted within two (2) years after the rejection. However, if the product is registered in the reference countries, submission of application can be made earlier.			NA	
Pre-approval inspection	GCP inspection		GCP on-site inspection is executed by provincial FDA for local manufacturing drug at principal investigator's site. GCP on-site inspection for import drug is not mandatory yet.	Not required	DCGI may conduct GCP on-site inspection. DCGI will issue instructions to the CDSCO officers/Inspectors to conduct the inspection identifying the clinical trial site/ facilities to be inspected. CDSCO issued 'GUIDANCE ON CLINICAL TRIAL INSPECTION' in Nov. 2010.	GCP inspection for local clinical study in Indonesia . GCP inspection for import product is not required.	The GCP on-site inspection is executed by PMDA to 2 or 4 medical institutions and applicants.	GCP on-site inspection to sites, company and CROs according to MFDS's yearly plan. Self-inspection by sites was adopted and is being implemented from 2012.	GCP Inspection extended to clinical trial sites and Sponsors; also planned for Contract Research Organisations (CRO) by 2015.	The GCP on-site inspection is executed by FDA to medical institutions and applicants. Frequency not clear.	CT in SIngapore Pre-marketing approval application inspections are usually done announced and apply to completed clinical trials. Criteria during GCP Inspections: (i)Protocol (ii)Medicines (Clinical Trials) Regulations (iii)SG-GCP, adapted from ICH E6 on GCP (iv)SOPs for conducting clinical trials	The GCP on-site inspection is executed by TFDA around 4-6 weeks after CSR submitted to TFDA in selected medical institutions (depends on the number of involved site)	

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Pre-approval inspection	GMP inspection	ex. On-site inspection, Document inspection, CPP/GMP certificate from source country accepted	For local drug, GMP on-site inspection should be done before manufacturing license approval. For import drug, CFDA started GMP on-site inspection at the end of 2011. Only few import drugs were selected at that time. Moreover, GMP on-site inspection was done after IDL approval at this moment, which is different from for local drug. It is sure that CFDA expects GMP on-site inspection prior to IDL approval once experience acuumulated. (IDL:Import Drug License)	Document inspection only, CPP/GMP certificate from source country accepted	GMP inspection of Indian mfg. units will be arranged before granting the manufacturing license and periodic review of the mfg. unit The Licensing authority or by any other persons to whom powers have been delegated in this behalf by the licensing authority of India may inspect the manufacturing premises of mfg. units outside India on need basis	For imported product : Based on evaluation of Site Master File , if necessary GMP inspection site will be request by NAFDC .	Since the amendment of the Pharmaceutical Law (PAL) in April 2005, GMP compliance inspections have become a requirement that must be met for marketing approval. Application for GMP compliance inspections for all manufacturing sites listed in the applicaitions for marketing approval must be submitted to the GMP compliance inspection authority (PMDA or prefectures) by each manufacturing site.	GMP inspection can be done for manufacturing sites of drug product and drug substance. Basically MFDS conduct on-site inspection (from 2009). Before conducting site inspection, they request "Minimum requirements" documents. Document inspection; inspected site within 1yr/aseptic product, 2yr/ sterile product, 3yr/ non-sterile product	For locally manufactured products, there is site inspection before issuance of GMP by the Health Authority. Foreign manufacturers are also subjected to GMP conformity assessments through acceptable GMP evidence or GMP inspection. For Imported products, on-site inspection are exempted for manufacturers from or inspected by PIC/s or reference countries, or from an ASEAN country included in the ASEAN Sectoral MRA for GMP inspection of manufacturers of Medicinal Products. All registration of imported products need to provide a GMP cert issued/inspected by member countries of PIC/S or reference countries.	Since 1989, GMP compliance inspections have become a requirement that must be met for marketing approval. For foreign manufacturer, CPP and GMP certificate is being required.	GMP conformity accessment is required usually in document review. GMP certificates must be issued by PIC/S member, US FDA and/or Japan MHLW. If not, onsite inspection by HSA Audit Branch required, before product approval is granted.	GMP on-site inspection or PMF registration (paper review) is requested and the approval should be got then NDA can be approved accordingly. Otherwise NDA Approval will be held until GMP sttus confirmed (inspection or PMF approval). The GMP compliance check should be done by TFDA for each manufacturing site, even toll manufacture site or packaging site.	GMP certificate (PIC/S) New foreign manufacturer may be inspected on site if needed.
	Other inspections	ex. GLP requirement and evaluation	For local drug, source data on-site inspection including GLP and CMC is mandatory after IND or NDA submission.	Not required	N/A	In the GMP inspection site , the Laboratory is inspected by NAFDC . The Laboratory inspected following GLP requirements.	"Paper-based compliance inspections" is executed by PMDA to confirm whether data attached to NDA applications accurately reflect the results of clinical trials and other studies, and whether those are made in accordance with GCP, GLP and reliability standards.	n/a	GLP Inspection of non-clinical test facilities is on-going. Subject to companies internal audit & ethics committees of the research institutions requirements.	Paper-based compliance inspections is executed by FDA to confirm whether good distribution practice is being implemented.	Non-clinical studies providing toxicology information to support clinical trials should be conducted in compliance with GLP.	Current Taiwan had not perform GpvP inspection. But the regulation for GLP site inspection already exists and some study will be performed GLP site inspection. As to the regulation related to GpvP inspection is under discussion.	

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Clinical trials	Necessary procedures to start clinical trials	The actual procedures to start clinical trials, for example, IND/CTA => import of investigational drugs => IRB etc.,	IND/CTA => import of investigational drugs and IRB => clinical trial clinical trial should be started within 3 years after obtaining CTA.	a. IRB approval b. if study medication is required to be imported, then Application of clinical trial certificate (CTC) at Drug Office, Department of Health is required	Clinical trial on new drug shall be initiated after authorization by CDSCO and approval of respective EC. In case of parallel applications, CDCSO will grant conditional approval and note that the trial should start after Ethics approval. Trials should also be registered with CTRI (Indian Registry) before screening patients	1. After having Clinical Trial Approval Letter from NAFDC, the Clinical Study can be start . Implementation of Clinical Trial.	Notice of claimed investigational new drug exemption to MHLW. Clinical trial can be started after 30 days if there is any comment from Authority	Get IND Approval and IRB approval in apparel. After that, it will be implemented CTA. Normally, it will take about 3 months.	Application to The Research Review Committee (RRC) & The Medical Research Ethics Committee (MREC) required. Also, application to the National Pharmaceutical Control Bureau (NPCB) for clinical trial import license is (CTIL) necessary. Parallel submission is possible.	Clinical Trial Protocol approval is required. Please see FDA Circular 2012-007 (flowchart).	Approval by both HSA (to obtain CTC) and IRB approval are required respectively before start of clinical trial.	IND approval by TFDA + Import permit of IMP → IND approval by IRB (IND in TFDA and IRB can be parellel) → CTA approval by medical insitiuation → Payment pay to medical institution completely →Site initiated visit.	IRB/EC approval -> Investigational drugs import approval from Thai FDA -> initiation
	Necessary data/ documents/ brochures to start clinical trials	Necessary Tox data for initiation of clinical trials (specify local requirement other than ICH-M3 or S6)	Protocol & IB. Usually TOX data aren't required for initiation of clinical trial because all data have been reviewed by authorities. Because site/IRB always follows CTA.	Please refer to the guidelines (file name: CT-guid)	List of necessary Tox data is shown in APPENDIX III of Schedule Y, the Drug and Cosmetics Rules 1945.	Clinical Trial Documents consist of : UK-1 Form, Protocol, Investigator's Brochure, Informed Consent, Documents of trial drugs, Summary Protocol of Batch Production (for Vaccine and biological products).	Generally we will follow ICH requirement. Sometimes add reproductive toxicity testings before clinical trials.	Mostly according to ICH requirements but regarding repeat dose toxicity in rodents, administration period is longer(6 months) than ICH guidelines(3 months). Sometimes add reproductive toxicity testings before clinical trials.	Submission of Investigator Brochure is required.	Generally follow ASEAN requirement. Please see FDA Circular 2012-007	1. Clinical trial protocol 2. Patient information sheet and ICF form. 3. Subject recruitment procedures and advertisements (if applicable) 4. Listing of overseas trial centres (if applicable) 5. Principal investigator(s) CV, GCP cert 6. GMP certificate or certificate of accreditation 7. CoA (if appicable) 8. Letter of approval issued by IRB 9. Other relevant supporting documents, if applicable 10. IB	It depends on the product characteristic and study phase. Some time Tox data may beneeded for initiation of clinical trials. General requirement also follows ICH guidance.	ICH E6
		Are there any necessary documents/brochures outside IND/CTA dossier	CRF & ICF Contract with site IRB approval Some sites require insurance certificate for the clinical trial	Please refer to the guidelines (file name: CT-guid)	As per Schedule Y Registration of clinical trial is mandatory in the ICMR Clinical Trial Registry prior to initiation of the trial.	Informed Consent to the patient	Documents needed to get patients' consent	CRF(Case Report Form), GMP warranty letter or certificate, documents to get patients' consent	refer to CTIL guideline	Documents needed to get patients' consent. Please see FDA Circular 2012-007.	Original declaration document of the principal investigator and sponsor has to be submitted	No extra document requires outside IND/CTA dossier. Only for biosample needs to send out to oversea, the statement from central lab is needed.	Material Transfer Agreement
		Document Language (acceptability of English document)	In Chinese.	preferably English and patients consent form in English and Chinese/Chinese only	English	Indonesian or English	Usually Japanese documents are requested	Protocol, ICF should be translated into Korean. However English IB is acceptable to MFDS.	English is acceptable. Note: Documents for patient - would need Malay, Chinese and Tamil	English	English	Usually English version is acceptable.	Thai and/or English
	Requirement of domestic clinical data for NDA application, if there is foreign data	Necessary or Not-necessary -Necessity in PK / healthy sbj. -Necessity in patient data	Usually Chinese patient's data including DB study and PK study are needed, which indicates similarity in drug response (i.e. efficacy and safety) with foreign data.	Not necessary	Necessary	Generally, Indonesian patient's data requested which indicates similarity in drug response (i.e. Efficacy and safety) with foreign data for new psychotropic drug, drug for family planning programme and other drugs based on request from Authorized body , for example public health programme for TB , etc.	Usually Japanese patient's data requested, which indicates similarity in drug response (i.e. efficacy and safety) with foreign data.	Foreign data is acceptable. But bridging data in Korean should be generated.	Not necessary	Local clinical trial is optional; PSUR submission will be required as part of Post-Marketing Surveillance.	Not necessary	If there is foreign data available, it doesn't need domestic PK data for IND application. But some situation may need domestic PK data for supporting NDA approval even there is foreign data approval, that is the product with ethical difference between Asis population and Caucasians.	Not-necessary
	Acceptance of foreign clinical data for NDA	Is there any conditional requirements, for example similarity in PK/PD?	No, just for reference. (Even if the similarity in PK/PD is indicated we can't rely only on foreign data to China NDA)	Yes (for NCE products) Not required for generic products	Foreign Clinical data can be a supportive document, however Indian data (PhaseIII) is must.	Acceptable if the clinical data following GCP and the result based on evaluation of safety and efficacy is good.	Acceptable if the similarity in PK/PD is indicated.	Acceptable; in case of similarity on S&E or PK/PD.	Yes	Acceptable if the similarity in PK/PD is indicated.	Yes	Acceptable if the similarity in PK/PD is proofed.	Yes
	Required number (or rate) of local subjects in pivotal clinical studies for NDA approval	Please explain for both local and multinational clinical trials, if necessary. ex. totally around 100 ex. 1/5 of all subjects in multi-national studies	At least 20-30 for Ph-1, 100 for Ph-2, 300 for Ph-3 in treatment group for local trial (for category 1 of chemical drug). For registration purpose, 100 pairs of Chinese patients in pivotal studies is requested whatever local studies or MRCT. Meanwhile, it is requested to show similarity in drug response and safety profile between Chinese and foreign patients in MRCT.	Not specified	P-I: 1-2 centers. At least 2 patients. P-II: 3-4 centers. At least 10-12 patients. P-III: a. The drug already approved/marketed in other countries: at least 100 patients distributed over 3-4 centres. b. The drug is a new drug substance discovered in India and not marketed in any other country: at least 500 patients distributed over 10-15 centres. (According to draft guideline) However Now a days DCGI asks for 200 patients or more for Phase III studues for the drug approved/marketed in other countries depending on the prevalance of disaese and therapeutics area.	Local clinical trial is needed for new psychotropic drugs .drugs for family planning programme, certain drug based on request from Authorized body.	It is requested to show the consistency in drug response between Japanese and foreign patients in multi-regional clinical trials. For this purpose, at least 15-20% of all subjects is hopefully to be Japanese.	No definite requirement. For both local and multinational clinical trials, statistically meaningful number of subject is needed.	N/A	There is no required number of local subjects in clinical trials for NDA approval. For PMS studies, it is suggested (but not required) that there should be 3,000 subjects. *Correction: PMS was not replaced but was expanded to include RMP /PSUR submission	N/A. But in the HSA CTC application, applicant has to declare expected number of subjects to be enrolled from each site.	it is request to show the consistency in drug response between Asia population and Caucasians in multi-national clinical trials. For this purpose, at least 15-20% of all subjects is hopefully to be Asian population. As for NDA approval, it was divided to two situation. Non-CPP: Early clinical development in Taiwan, Ph 1+ Ph 3 or Ph 2+ Ph 3.Taiwan patient No. for Ph1 study : ≧10, for Ph 2 study: ≧20, for Ph3 study: ≧80. One-CPP: One of Ph 1, Ph2 or Ph3 study in Taiwan. Taiwan patient No. for Ph1 study : ≧10, for Ph 2 study: ≧20 or 10%, for Ph3 study: ≧80 or 10%, or Multinational Ph3 study: total sample size ≧200 then Taiwan No. ≧30 or 5%, total sample size ＜200 thenTaiwan No. ≧10.	Not-necessary

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Clinical trials	Practicable number of clinical centers or sites in the country	# of sites with facility of clinical trials Is there any license system for clinical study site?	Involved clinical center or site should get a license of CFDA. More than 300 sites/hospitals are qualified by CFDA.	Practicable no. of clinical study sites not specified; No license system for clinical study sites; however, the clinical study sites are usually university or government hospitals.	Not specified.	It around 50 clinical centre .	Clinical trial can be initiated in many study sites. No license system for clinical study sites.	Certified sites by MFDS: 156 sites(Sep. 2012)	CRC(Clinical Research Centre) controls 17 clinical centers, 50 hospitals and 100 clinics.	Clinical trial can be initiated in many study sites. No license system for clinical study sites but the protocol should be evaluated by IRB/EC.	There are 13 public hospitals and 16 private hospitals which can conduct clinical trials.	More than 100 hospitals can conduct clinical trials including 19 medical cenenters. (Delete "38 clinical sites get confirmation by TFDA for IRB certification and allow these 38 IRBs can do review and approve without TFDA approval. " since this announcement has expired. 78 Valid IRB name list is as "TFDA Certified IRB list" file 4. 78 of them have valid IRBs per TFDA inspection result. There is no license system for evaluate clinical study sites.	8 officially recognized sites (IRB/EC site) No (Beware of USFDA blacklist)
	IRB system for clinical trials	Installation of IRB/EC in sites Is there National IRB?	IEC at each site	Yes. An IRB for each cluster of hospitals	Independent Ethical Committee (IEC) & Institutional Ethics Committee	There are National IRB system .	Institutional IRB.	Institutional IRB	institutional and national IRB (MREC) available depending on sites	Institutional IRB/Ethic Committee. The general guidelines on CT may be referenced from the "National ethical Guidelines for Health Research 2011 edition. Another reference is FDA Circular 2012-007 that recognize ERB/ERC for purposes of conducting CT of Investigational Medicinal Products and it also validates the agreement between the FDA and PNHRS or Philippine National Health Research System which includes the establishment of a clinical trial registry.	Singapore has 2 clusters of public hospitals. 1 cluster is under NHG DSRB (National Healthcare Group Domain-Specific Review Board) and the other cluster is under SingHealth CIRB (Centralised Institutional Review Board). For private hospitals, they have their own IRB/EC	c-IRB is composed of 18 hospital IRBs. Some other sites may also take fast track for c-IRB approved trials. JIRB covers 85 hospitals. (this information is collected from C-IRB website) Every medical center has its own IRB. There is different requirement between different IRB.	available Yes, National IRB or Central IRB.
	Prevalence of GCP in clinical centers		GCP is observed in all clinical sites.	Yes	Yes. GCP is observed in all clinical sites.	GCP is observed in all clinical studies	GCP is observed in all clinical sites.	GCP is observed in all clinical sites. Same as Japan.	GCP is observed in all clinical studies. (Local recognized GCP certificate is compulsory for all investigators.)	Yes, GCP is observed in all clinical sites. ICH Guidelines, GCP E6	GCP is observed in all clinical studies	GCP is observed in all medical center and teaching hospital.	a must
Clinical trials	Investigators	ex. about 50 physicians have been trained in US/EC	uncountable number of physicians in China.	Yes	Large pool of trained Investigators in diverse therapy areas	Investigator must have GCP training before the trial and understand the protocol comprehensively in order to conduct the trial in accordance to GCP. No requirement investigator have been trained in US/EC.	uncountable number of physicians in Japan	uncountable	Information not available	Uncountable number of physicians. In addition to CVs, IRBs require that investigators undergo GCP training and this should be renewed or refreshed every 2 years.	No info	TFDA regulated necessary training hours needed for GCP and ethical then qualified to conduct clinical trial. No actual number of investigator to get GCP training.	no information (Beware of USFDA blacklist)
	Investigational drug	Condition of customs procedure	Tax and custom clearance. If imported investigational drugs to be used, CTA is necessary for Customs procedures and clearance.	Application of Import License based on the approved CTC	Permission to import of investigational product shall be obtained by applying for a test license. The application should be made in Form 12.	Sponsor request to import unregistered product was to NAFDC. Approval letter for Importation from NAFDC is used for release product in the customs . .		After the IND approval. Import permit should be gotten from Korea Pharmaceutical Traders Association in advance.	clinical trial import license and proper clearance required	yes	Application for Import License of CTM required. Online application is possible. Can import less than the amount approved in the CTM, but not more. The approved CTM form needs to be submitted to the Trade Net office for custom clearance.	It needs to get import permit that issue from TFDA, then Customs will allow investigational product import into Taiwan within the quantity on the import permit.	Condition of customs procedure - import license, CoA, Airway bill, invoice
		Investigational drug labeling (requirements and language)	Chinese label is needed.	IP name; Strength, dosage, storage condition; manufacturer - English or English and Chinese	• "For Clinical Studies only" • Name or a code number of the study • Name and contact numbers of the investigator • Name of the institution • Subject's identification code	In Indonesia language for clinical trial in Indonesia.	Japanese label is needed	Korean label is needed Requirements : 1) Investigational use only statement 2) Code name or generic name 3) Lot/batch number, expire/retest date 4) Storage condition 5) IND holder's name and address 6) "It can not be used for other purposes except clinical trial" statement	refer to CTIL guideline. English acceptable	yes, in English	1. Designation or other identification mark on each item of such material. 2. Name/address of manufacturer. 3. Batch number. 4. Name or other identification mark of the subject. 5. Manufactured date and expiry date. 6. Storage condition. 7. 'The product should only be used under strict medical surveillance' ; and/or "for Clinical Trial Use only" 8. Must comply with GCP labeling requirements.	Traditional Chinese label is needed.	Require local language with product name or random number, dosage, amount, manufacturer, expired date and the content of 'this product is used for clinical trial only'.
	Investigational drug	Usability of an unapproved drug as a comparator	No (almost impossible).	Yes	No	Unapproved drug should provide data as below: Quality Data, Investigator's Brochure, and Summary Report of Non -Clinical & Clinical data, Summary of Batch Production Report (for Vaccines and Biological Product)	It is possible to use an unapproved drug as a comparator if the unapproved drug is the international standard drug. It is recommended to gather relevant safety information of the unapproved drug in Japanese.	Possible if the unapproved drug is the international standard drug. It is recommended to discuss with MFDS in advance.	depend on protocol design and supporting documents provided. E.g. drug approved in another country and not MYS, should be acceptable as long as required supporting documents (e.g. safety data) provided	It is possible to use an unapproved drug as a comparator if the unapproved drug is the international standard drug. It is recommended to gather relevant safety information of the unapproved drug.	As long as protocol and CTC approved, can be used	It is possible to use an unapproved drug as a comparator if the unapproved drug is the international standard drug. It is recommended to gather relevant safety and efficacy information of the unapproved drug in English.	Possible subject to IRB/EC approval

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	Export shipment of bio-samples from subjects	ex. possible, can be measured at Central Labs.	There is specific regulation for export of human samples. Samples can be exported after approval.	Possible	Possible	There are Regulation no 657/MenKes/Per/VIII/2009 for export shipment of bio-samples from subject. The request for export of bio-samples to Ministry of Health.	Samples can be exported	Samples can be exported	samples can be exported. Export permit required	Possible, can be measured at central laboratory	Can, as long as meet the importing countries necessary requirements. It is the applicant's responsibility to comply with importing country's requirements	Possible, can be measured at Central labs. But it needs statement from Central lab, also the information for the Central lab needs clarified in the statement in detail, ex address, contact window. If central lab is located in foreign, Sponsor/ central lab's warrent letter for export of sample (which is not dislinkage) is needed to obtain IRB and TFDA approval. according th TFDA annoucement regulation on Dec 28, 2011, (human research law). For Biogene sample, it needs to indicate the test gene information in advance then can allow to export.	Possible (MTA required by most IRB)
Clinical trials	Availability of multi-national CRO	ex . ** has local branch, many local CROs	Multi-national CRO is available in China, such as Quintiles, ICON, Covance, ICN, PPD, PRA, RPS etc	Yes (domestic and multi-national companies)	Multi-national CROs like Quintiles, Parexel, PPD, ICON etc are available	Multi-national CRO is available in Indonesian.	multi-national CRO is available in Japan	There are many multi-national CROs branch. Many local CROs.	available	Multi-national CRO is available in Philippines	Available	Multi-national CRO is available in Taiwan	Approximately 10 CROs available
	Adverse reaction reporting during clinical trial	ex . SAE: report to Authority within 7 days etc.,	SAE: it is requested to report to the relevant authority in 24 hours after knowing the event.	Serious and unexpected adverse events - Fatal/life threatening: no later than 7 calendar days; submit report in 8 additional calendar days - Others: 15 calendar days NSAE and serious expected adverse events: - Brief summary at the end of trial	As per new Gazette GSR 53(E)passed by Govt. of India on 30 January 2013, Any report of serious adverse event of death occurring in clinical trial, after due analysis shall be forwarded by the Sponsor to Chairman of the Ethics Committee and Chairman of the Expert Committee constituted by the Licensing Authority as defined under rule 21(b) under Appendix XII with a copy of the report to the Licensing Athority and the head of the Institution where the trial has been conducted within ten calendar days of occurrence of the serious adverse event of death. The report of the serious adverse event other than death, after due analysis, shall be forwarded by the Sponsor to the Licensing Authority, Chairman of the Ethics Committee and the head of the Institution where the trial has been conducted within ten calendar days of occurrence of the serious adverse event.	Investigator should report all serious unexpected adverse event to sponsor /CRO as soon as possible after known it, if there are some next adverse event, report a.s.a.p. until end of event. Sponsor should report all serious adverse event in Clinical Trial include death to Head of NAFDC and Ethics Committee within 15 days start from known the event , if there is next event, report it a.s.a.p until end of event.		Report SUSAR to MFDS within 7 days : Death, life-threatening within 15days : other SUSARs	refer to CTIL guideline	SAE: report to Authority within 3-7 days. Please see FDA Circular 2012-007 (p.9-10)	Fatal or life-threatening unexpected ADRs: within 7 calendar days. All other serious unexpected ADRs: within 15 calendar days. (See Guidance for Industry: Safety Reporting Requirments for Clinical Drug Trials)	SUSAR: report to Authority within 7 days for death and life threatening case, within 15 days for other cause. It is same as international rule.	To FDA: Only SAE related to product report to FDA, death or life-threatening related to study product within 7 days, other SAEs within 15 days, AE at the end of study. To site IRB/EC: Death or life-threatening within 24 hours, other SAE within 7 days, AE at the end of study.
	GCP site inspection			Accreditated to the sites by separate parties	Yes.				Yes		Will be conducted by the HSA Clinical Trial Branch, on locally conducted clinical trials.		Yes

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Manu-facturing	Acceptance test for Import drug	How the specifications & test methods for acceptance test of import drugs are set in your country?	Specifications and test methods are to be set according to quality verification test done by authority and Ch.P. (Chinese Pharmacopoeia).	Based on the approved particulars.	Specifications and test methods are to be set according to registered specifications. Official in pharmacopoeia or in-house specifications with validation data are available.	Specification and test methods are following Indonesian Pharmacopoeia, USP, BP, or other Pharmacopoeia.	Specifications and test methods are to be set according to JP.	Specification and test methods are usually set in accordance with official compendium or registered in-house specifications.	The latest version of British Pharmacopoeia (BP) and United State Pharmacopeia (USP) shall be used as the main references. All tests and its specification listed in BP and/or USP shall be the minimum requirement. However, a specific testing method for quantitative analysis shall be accepted. All test specifications set by the manufacturer shall be in line or more stringent than official pharmacopoeias (BP and USP). The specifications can be set by company, as long as it is aligned with the international reference & approved by the reference countries. Full validation for in-house methods is required. All the analytical validation done by the industry should be in accordance to ASEAN Guidelines for Analytical Procedures, ICH Technical Requirements for Registration of Pharmaceuticals for Human Use under Validation of Analytical Procedures: Text and Methodology Q2 (R1), British Pharmacopoeia (BP) or United State Pharmacopeia (USP).	Specifications and test methods are to be set according to registered specifications. PFDA has adopted the implementation of the ACTD in submission of registration of pharmaceutical prooducts but there is flexibility in the use of ICH dossier even for generic drugs.	To be tested according to approved specifications & test methods	Specification and test methods are to be set according to international pharmacopoeia, like JP, EP, USP/NF. For innovative product, it is allow to use Company Own specification and test methods with validation data and scientific justification.	Both compendial and non-compendial method are acceptable
	Pharmacopeia	What is standard pharmacopeia ? What is other accepted pharmacopeia? ex. USP/NF, JP, EP	Ch.P.	BP, USP, EP and JP. In-house specification for NCE would be accepted by DOH.	If a DP/DS is official in the Indian Pharmacopoeia(IP) than must conform to IP if not official in IP than BP/USP/EU Pharmacopoeia standards are to be followed	Standard Pharmacopoeia : Indonesian Pharmacopeia Other accepted Pharmacopoeia : USP/NF, BP, EP, JP.	JP (Japanese Pharmacopeia)	Standard : KP Accepted : JP, Ph. Eur(EP), USP(NF), BP, Deutshces Arzneibuch, Pharmaacipee Francaise	The main pharmacopieal references are BP and USP. Others are JP and EP.	JP, USP/NF, EP, BP, PP (Philippine Pharmacopoeia)	BP, EP, USP/NF JP (chemical drugs and excipients)	Accepted pharmacopoeia are JP, EP, USP/NF.	USP 34, NF 29 and supplements, BP 2011 volume 1-5 and Addenda, the fourth edition of IP and supplements, Thai-pharmacopoeia II volume I part 1 and supplements, the seventh edition of EP and supplements
	GMP system	What is current GMP requirements? ex. PIC/S	Chinese GMP 2010 version(MOH order 79)	PIC/S has been adopted for local manufacturer licensing PIC/S would be adopted for overseas manufacturer within a few years.	Indian GMP as outlined in Schedule M of DRUGS AND COSMETICS RULES, 1945 Then, these regulations and guidelines (Schedule M) were revised in order to be based on WHO-GMP in 2003.	PIC/S GMP requirements	Japan applied for membership in the PIC/S GMP (March 2012)	KGMP Korea applied for membership in the PIC/S GMP(May 2012)	The current PIC/S Guide to GMP for Medicinal Products and its Annexes have been adopted as the standard used by NPCB to assess the GMP conformity of manufacturers.	Philippine applied for membership in the PICS (June 2010) --> PFDA has adopted the PICs Guidelines for GMP of medicinal products as per AO 2012-0008	PIC/S GMP requirements	Taiwan is PIC/S member since Jan 2013.	Under application for PIC/S membership.
Manu-facturing		Please describe GMP evaluation process by the authorities. ex. GMP clearance/ accreditation required before NDA ex. On-site or document inspection ex. Acceptability of GMP certificate from original country	1)For local drug, GMP compliance is pre-requisite for obtaining a Product Marketing Approval in China (see "NDA" - GMP inspection). GMP inspection to licensed manufacturer is carried out every five years by on-site inspection. And the application for GMP renewal should be submitted 6 months before GMP expiration. 2)For import drug, GMP on-site inspection has been started recently. So some import drugs were selected for GMP inspection to abroad site and it were done after license approval.	For overseas manufacturer, inspection is usually not required. For local manufacturer, an inspection by pharmacist inspector will be conducted at the company's premises within 2 weeks from the submission of a new application. The application will be considered by the committee. If approved, a license valid for 1 year will be granted.	GMP inspection will be arranged before granting the manufacturing license and periodically The Licensing authority or by any other persons to whom powers have been delegated in this behalf by the licensing authority of India may inspect the manufacturing premises of mfg units outside India on need basis.	The manufacturer which is first time register export product to Indonesia should provide SITE MASTER FILE (SMF) for GMP evaluation. After evaluation of SMF, the NADFC will approve to continue registration process of NDA or request site inspection. Before inspection, the manufacturer should provide Pre-inspection document for preparation of the site inspection . After inspection, the NADFC will issue approved or reject to continue registration NDA. The inspection report from other Authorized Health Authority is needed to support evaluation of SMF.	GMP compliance is pre-requisite for obtaining a Product Marketing Approval in Japan (see Pre-approval inspection, GMP). GMP inspection to licensed manufacturer is carried out every five years either by on-site or document inspection.	Pre-approval GMP review: 1) documents (Minimum requirements) -based 2) Site inspection. In case MFDS visits the same site within 3 years for another products which used the same manufacturing method, on-site inspection could be waived. (In case of biologics, exemption period is maximum 2 years.) Even though MFDS does not visit the site, documents for GMP review should be submitted. 3) Supplementary request after site inspection	<u>For locally manufactured products</u>: Site inspection is required before issuance of GMP cert. <u>For imported products</u>: On-site GMP inspection is required to ensure the conformance of foreign manufacturers to GMP requirements and standards for products that are registered or that are undergoing the registration/re-registration/change of manufacturing site process and those products manufactured for clinical trial purposes (investigational medicinal products). However NPCB will accept documentary evidence of GMP conformance of a manufacturer located outside Malaysia on the following condition: The GMP evidence is issued by a PIC/S Participating Authority or an ICH member country Competent Authority following an on-site inspection conducted by the authority; OR The GMP evidence is issued by a Listed Inspection Service under the ASEAN Sectoral Mutual Recognition Arrangement for Good Manufacturing Practice (GMP) Inspection of Manufacturers of Medicinal Products. The acceptable GMP evidence shall be in the format of a GMP certificate or GMP inspection report. Where acceptable GMP evidence of the foreign manufacturer is not available, or where the documentary evidence submitted is insufficient to demonstrate acceptable GMP standard, a GMP inspection has to be conducted on the manufacturer by NPCB. Nevertheless the availability of acceptable GMP evidence does not preclude NPCB from carrying out the GMP inspection on the manufacturer.	GMP compliance is pre-requisite for the site registration of the manufacturing site and source into the License to Operate, which then is a requirement in obtaining a Product Marketing Approval in Philippines. Current evaluation for foreign sites is based on documentation review. GMP inspection of licensed local manufacturer is conducted by local FDA every 2 years, either by on-site or document inspection. Implementing guidelines for the Foreign site GMP audit is still in-progress.	Domestic manufacturers in Singapore are subjected to licensing and periodic GMP audits by HSA. All new overseas manufacturers will be subjected to a GMP Conformity Assessment by HSA. Refer to Guidance Notes on GMP Conformity Assessment of an Overseas Manufacturer (Dec, 2008)	GMP compliance on-site inspection is pre-requisite for NDA approval for new manufacturing site. The already registered manufacturing site should be get routine GMP renewal (follow up management) through onsite inspection or document inspection every 2 to 4 years depends on the first approved expiry date.	GMP accreditation is required for new site, which has never been registered in Thailand. GMP accreditation is allowed to be submitted on parallel with product registration, but GMP must be accredited prior product license issuance. GMP license will last 2 years, but the site may be inspected earlier than 2 years depending on the judgment of the FDA inspector.

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Manu - facturing		Please describe frequency/number of on-site inspections to domestic/overseas manufacturers by the authorities. ex. number of inspections conducted in last year	At the end of 2011, 7 GMP on-site inspections to overseas manufacturers were conducted. The situation of 2012 and 2013 is unclear, but GMP on-site inspections to overseas manufacturers is announced to be conducted in 2014. GMP on-site inspection to domestic manufacturers were 126 in 2011, and it were 141 as of 30th Nov. 2012.	Since the manufacture license valids for only 1 year, inspection will be made at least on annual basis for local manufacturers	Annually. For overseas, CDSCO started inspection of Pharmaceutical firms for import registration of drugs. Six on-site inspections in 2011 for DS manufacturing site in China, and four China drug manufacturing sites in 2012.	Every month there are on site inspection to domestic and overseas manufacturers by the Authorities. Almost Asia countries are inspected.	Number of on-site GMP inspection to overseas manufacturer in FY 2012 was 66. About 60% are in Asia. On-site inspection to Japanese domestic manufacturer by PMDA in FY 2012 was 132.	Number of on-site inspection to overseas manufacturers in 2011 was 90. Domestic manufactures in 2011 : 232 by MFDS (90 by other authorities, e.g. FDA, EMA)	Inspection is required for products that are undergoing the registration/re-registration/change of manufacturing site process and those products manufactured for clinical trial purposes (investigational medicinal products). Domestic manufacturers are inspected at least once a year for annual manufacturing license. *In 2012, a total of 299 GMP inspections were conducted.* *The GMP inspections comprises of routine and nonroutine inspections of manufacturer premises from various categories such as pharmaceutical, traditional, cosmetics, veterinary, active pharmaceutical ingredient (API) and others. From the total 299 inspections, the number of inspections conducted in premises of cosmetics, traditional, pharmaceutical and others (veterinary, API, stem cells and etc.) are 119, 102, 45 and 33 respectively.*	No details as of this moment.		TFDA: domestic: about 180, overseas: about 30 (in 2012).	- Domestic: Non- sterile drug: every 3 years Sterile drug: every 1.5 year - Overseas: if needed FDA's plan on inspection: (Note: The FDA is working on the update of this regulation, but not come out yet at time of report) • Routine Inspections ~ 60-70 plants/year • Special inspection in special case • And there will be Follow up Inspection which they are setting on criteria (may be from Risk Assessment).
	DMF system	Please describe DMF system (or plan for introduction). Is DMF mandatory or optional?	DMF system is investigated but not yet implement.	Not specified	No DMF system exists. (Note: CMC part of application dossier is called DMF, but it does not mean DMF system as in other countries.) API DMF as per ICH CTD is also acceptable.	DMF is required for new active substance.	The submission of MF (Master File) is optional. Drug substance, Intermediate, New excipients, Packaging materials etc. are subjects of MF.	NCE and API for generics should be submitted DMF since 2002. But all APIs should be registered by 2015. (Every year, MFDS announced the list of APIs which should be registered.) Only drug substance(API) is subject of DMF.	A DMF is required for API registration, starting with Phase 1 for NCE registrations in Jan 2012. This may be replaced by a CEP or full details of Part II S ACTD. Regulatory control of active pharmaceutical ingredient (API) is applicable to all pharmaceutical products either locally manufactured or imported, excluding biologics, health supplements and natural products. Phase 2 will also be implemented for Generics (Scheduled Poison) as given below: New Generics: Parenterals by 1 July 2014, Oral dosage forms by 1 July 2016, All other dosage formsby: 1 July 2018 Existing Products: At registration renewals for Parenterals by 1 July 2015, Oral dosage forms by 1 July 2017, All other dosage forms by 1 July 2019. (Submission of required documents to be done 1 year before product licence expiry.)	DMF system is recognized as per adoption of ASEAN Variations Guideline.	Yes. It is optional to use DMF in application submission. DMF Submission FORM in Appendix 18(effective 1April 2014. See UPDATE Jan 2014: Guideline on Medical Ptroduct Registration in Singapore)	Current only DMF regulation for drug substance available. But now it is no mandatory request for all API. TFDA will announce the product list for DMF compliance in next year. It may effective since year 2016 for all API. The 1st stage DMF management regualtion is announce on May 21, 2013.	No DMF system
	DMF system	Annual or periodical update reporting required?	not yet implement.	Not specified	N/A	N/A	No annual updated system. Partial change application or notification is required for changes.	Annual report should be submitted by Jan. 31 every year if the relevant changes are applicable for the subject of annual report	Manufacturers of finished products should establish a mechanism by which manufacturers/suppliers of an API shall provide information on any changes (i.e. variations) in manufacture and control that may have impact on the safety, purity and quality of the API. It is the MAH's responsibility to provide the Agency with the appropriate documentation (referring to relevant parts of the dossier) to prove that any intended or implemented variation will not have an impact on the safety, purity and quality of the API that has been previously approved. The NPCB may conduct a re-evaluation of the APIs at a 5 year interval.	Updating of DMF depends on post-approval applications as per the ASEAN Variations Guideline	Applicants are responsible to maintain and update the DMF. When a DMF has been updated, the DMF Submission Form and a summary table of changes made in the DMF update must accompany the updated sections of the DMF. If there are changes to the DMF that will result in a post-approval variation to the drug product, applicants must file a post-approval variation	No annual updated system. Partial change application or notification is required for changes.	Not required

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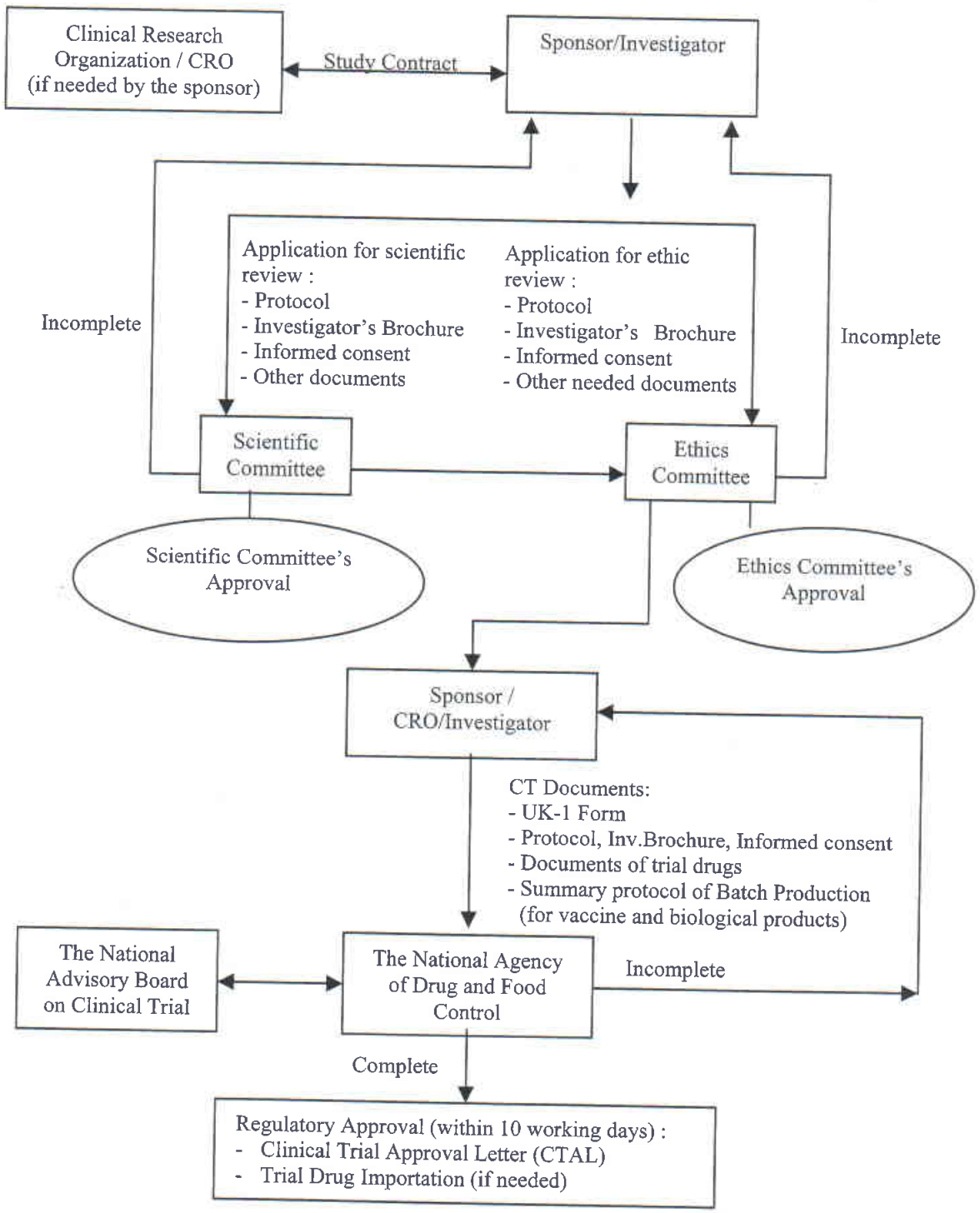
Manu-facturing	Contents of packaging label and language	Please describe required contents of packaging label and language to be used. ex. refer to guidance document	The required contents are described in CFDA order 24. The contents should be written in Chinese.	English or English and Chinese, requirements decribed in Guidelines on the Labelling of Pharmaceutical Products	The required contents are described in rule 96 & Schedule D2 of the Drug and Cosmetic Rules 1945. PI and packaging labels should be written in English.	New guideline 2011 for labeling prescription drug : request to provide Package insert (English or Indonesia), Patient Information Leaflet (Indonesian), outerbox should following packaging requirement (name of the product, active substance, volume, indication, contraindication, dosage and administration, storage condition, manufacturing name & address , imported by,) also retail price, Registration number, Harus dengan resep dokter, Logo of prescription drug. In the label, after product name should follow active substance names, Label also following regulation on registration. Guideline for OTC : inner box and all product information should be in Indonesian language.	The required contents are described in Article 50 of the Pharmaceutical Affairs Act. The contents Should be written in Japanese.	Language : Korean Requirement : Follow Article 56 of the Pharmaceutical Affairs Act and in Act Article 69 of the Enforcement Regulation on the Safety of Pharmaceutials etc..	The labeling content is stated in Drug Regulatory Guidance Document. The labeling for pharmaceutical products are in English or Bahasa Malaysia. Some labelling statements are mandatory in Bahasa Malaysia, eg for "Keep medicine out of reach of children".	The required contents are described in Generic Labeling Law. The contents Should be written in English. (see A.O. 55, series 1988)	Refer to: GUIDANCE ON MEDICINAL PRODUCT REGISTRATION IN SINGAPORE APPENDIX 6 POINTS TO CONSIDER FOR SINGAPORE LABELLING	The required contents are described in Article 20 of "drug review and registration guideline". The contents should be written in English and Chinese.	Follow ASEAN labeling requirements Thai language required for - category of drug - expiration date - special warning
	Bar code on packaging materials	Please describe requirements of Bar Code on packaging materials and concerned regulations.	Bar code on packaging material for national essential drugs should be completed by Feb. 2012, while the deadline for whole drugs is by Dec. 2015.	For product registration, no concern. For supply to government hospital: GTIN barcode as issued by GS-1	For product registration, no concern. For supply to government hospital: GTIN barcode is required Barcode requirements using GS1 identification standards has been implemented. (reference: The Office Memorandum No: Z-16025/02/08-EPW dated 6th May 2011 by MoHFW). For local Indian market, it is still not made mandatory.	No regulatory requirement on bar code. It is an internal company logistics requirement.	The contents Should be written in Japanese.	Requirement : Article 75 of the Pharmaceutical Affairs Act. Article 69 of the Enforcement Regulation on the Safety of Pharmaceuticals etc. & Notification on the Use and Mamnagement of Drug Bar Codes and RFID tags GS1-128 barcode system (GTIN-13 Product code + expiry date + Batch No. + Serial No(in the case of Serial No., it should be applied as of Jan. 2015.) should be used.	Bar code is an optional information.	Barcode is required per SKU. It is not a regulatory requirement but more of a marketing or trade requirement.	No regulatory requirement on bar code. It is a internal company logistics requirement.	Current barcode labeling of product code is required to manufacturers/distributors depending on package unit (carton) or outer box. Barcode regulation on product unit (per tablet for blister, per bottle, per vial for injection) is draft and under discussion. The requirement for the barcode will be GTIN(GS1) data matrix.	No regulatory requirement for Bar code But some hospitals require barcode.
	Renewal system of approved license	Please describe renewal system of marketing authorization or manufacturing license. ex. renewal required every 5 years ex. re-evaluation system	Manufacturing license system is adopted for drug administration. So, renewal system is based on manufacturing license. Renewal is required every 5 years, and should be submitted within 6 months before expiration date of license.	Renewal required every 5 year.	Renewal system has been implemented for the followings. 1) Import license (Every 3 years. Renewal application should be made three months before the expiry of the existing license.) 2) Registration certificate (Every 3 years. Renewal application should be made nine months before the expiry of the existing license.) 3) Manufacturing license (Every 5 years. The license will be expired if the renewal applications not made within six months of its expiry) Marketing Authorization is one time issue, no renewal required.	Marketing Authorization: Required every 5 years. Renewal application needs to be submitted 6 months prior to registration expiry. If needed, the NADFC will do re-evaluation system. Manufacturing License: Required every 5 years of every GMP facility and dosage form. Sometimes the NADFC will inspect the GMP facility before giving the renewal of Manufacturing license.	Not renewal but re-examination system is adopted. Drug monitoring is required for 8 years for NCE drug, 4-6 years for new indication/ administration route and 10 years for orphan drug.	Renewal system of approved licenses will be implemented from drugs which would be approved in 2013 (applicable for existing drugs as of Jan. 1, 2018). Documents should be submitted : 1) Summary reports on Safety and Efficacy of the drug product including the last 5-year 2) Usage in foreign countries, Any action related to safety in foreign countries 3) Data on Product Quality 4) Safety update report 5) In case anything would be changed from approval, its evidential data 6) Document on Drug Display (Label in carton, PI and so on) 7) Manufacturing or Importing records during the last five-year 8) Product Permission letter issued by MFDS	Renewal is required every 5 years of a product registration. Renewal needs to be submitted 6 months prior to registration expiry. Additional Notes for renewal requirements: NPCB will also require Zone IVb stability data to be updated during renewal review; however grace period for compliance has been allowed until Jan 2016. For renewal of imported products from Jan 2014, a GMP inspection is also required where acceptable GMP evidence of the foreign manufacturer is not available, or where the documentary evidence submitted is insufficient to demonstrate acceptable GMP standard. API registration for products containing "scheduled poisons" will be required before renewal, i.e. for Parenterals by 1 July 2015, Oral dosage forms by 1 July 2017, All other dosage forms by 1 July 2019. (Submission of required documents to be done 1 year before product licence expiry.)	Renewal system is being implemented. Renewal for products under Monitored Release status is after 3-5 years. Products on regular registration status, i.e. under Initial or Renewal status, renewal is done every 5 years. The PFDA is now controlling the renewal of licenses of non-marketed products.	Product licenses should be renewed every 12 months. Auto renewal system is implemented since 2009.	Renewal system of approved license is existed. The approved license needs to be renewed every 5 years.	There are 3 kinds of license in Thailand which are Manufacturing license, Import license and Sale license, all of which require annual renewal. Based on current Thai Drug Act, the product license is life-long, no requirement of renewal, except for drug classified as narcotics and psychotropics shall subject to renewal every 5 years.
Post approval	Post marketing surveillance or safety monitoring program	PSUR submission required? Other post-approval safety requirements? ex. Safety monitoring program/monitored release	PSUR submission is mandatory annually until the first renewal date and every 5 years after the first renewal date. Special monitoring over drugs within the new drug observation period as well as drugs imported for the first time within 5 years is mandatory performed. The monitoring results shall be summarized, analyzed, evaluated and reported as required.	For NCE only. PSUR has to be submitted every 6-monthly for the first 2 years of product registration approval, and annually in the following 3 years.	PSUR submission is mandatory for a period of four years. For new drug, every 6 months for the first 2 years, and annually for another 2 years. May be extended by the authority in the interest of public health. (Reference: Schedule Y of the Drugs and Cosmetics Rules amended in 2005) PSURs due for a period must be submitted within 30 calendar days of the last day of the reporting period.	PSUR submission is required only for NCE and certain product if it is required by HA. There is an obligation to report all Adverse Events (unexpected/expected , serious/ non serious in Indonesia or foreign countries) to NADFC .	PSUR submission is mandatory every 6 month in first two years and annually after two years. Use-result survey data should be submitted together.	PSUR submission is mandatory every 6 month in first two years and annually after two years. Use-result survey data should be submitted together.	PSUR is mandatory for NME: 6 months once in the first 2 years, and 12 months once in the subsequent 3 years.	As per PFDA Circular 2013-004, after the issuance of MA, the MAH shall submit a PSUR regularly to the FDA. When PBRER is part of the RMP, it shall also be submitted to the FDA. In general, a PSUR and/or PBRER shall be submitted at least once a year. Prompt and regular, or periodic submission of PSUR, PBRER, ICSRs,and spontaneous ADR reports shall constitute PMS activities.	When requested by HSA, PSUR should be submitted 6 months for the first 2 years, and 12 months for the subsequent 3 years. Ad-hoc submission requests can be raised if required.	PSUR submission is mandatory every 6 months in first two years and annually after two years. For NCE product, it necessary to submit PSUR in first 5 years. Other post approval safety requirement like RMP/REMs will be initiated by TFDA or Pharmaceutical company, it depends. For non-CPP NDA submission case, it is mandatory requirement to submit RMP/REMs together with NDA submission. For one-CPP NDA submission case, it may request by TFDA after their evaluation.	Yes, T-FDA requires PSUR for unconditional approval of New drug. SMP (Safety Monitoring Program) for NCE is required under conditional approval for 2 years.

Item	Contents	Detail or Example	China RDPAC	Hong Kong HKAPI	India OPPI	Indonesia IPMG	Japan JPMA	Korea KPMA/KRPIA	Malaysia PhAMA	Philippines PHAP	Singapore SAPI	Taiwan IRPMA	Thailand PReMA
	Risk Management Plan (RMP)	Please describe requirements of RMP/REMS. ex. Mandatory at NDA, submit up on request from the authorities	Not yet officially implemented. For the product which is accepted for special review procedure, Risk Management and Implementation Plan should be submitted at NDA.	One of the mandatory requirements for NCE registration	N/A at present	Not required yet. RMP regulation will establish later on.	RMP document is mandated for NDA as M1.11.	MFDS has a plan to adopt REMS within several years.	Not a mandatory requirement. May be required on request by the authorities, in particular for biosimilar/biological products.	N/A at present. A RMP is a requirement for the issuance of appropriate authorization & shall be one of the requirements when applying for marketing authorization application. It should be proportionate to the risks as shown by clinical evidences& the risk profile of the product. There is no specific format for RMP issued by the PFDA.	When available, RMP/REMS submitted to EMA/US-FDA may be requested at NDA, The need to implement a risk management plan in Singapore would be assessed on a case-by-case basis during the review process.	Mandatory at NDA for non-CPP product, submit up on request from TFDA.	Require for some specific group. Ex. Thalidomide .
Post approval	Adverse drug reaction reporting after marketing	Please describe reporting requirements of ADR for marketed products.	Reporting is mandated for ADR observed in post-marketing products including PMS. Reporting period of Serious ADR and expected ADR are within 15 days (30 days for non-Serious ADR for drugs within the new drug observation period or imported drugs within 5 years from the date of initial import permission).	For generic products, reporting is by means of voluntary basis. For NCE, SUSARs have to be reported within 15 calendar days from date of first receipt.	Serious unexpected adverse reactions: must be reported to the licensing authority within 15 days of initial receipt of the information by the applicant. Other: to be reported in PSUR.	Reporting is mandated for ADR observed in post-marketing products. 1. AE Spontaneous serious unexpected in Indonesia , as soon as possible, not more than 15 calendar days. 2. AE spontaneous non-serious unexpected in Indonesia, report every 6 months. 3. AE Spontaneous serious expected in Indonesia, as soon as possible, not more than 15 calendar days. 4. AE spontaneous serious unexpected in froiegn countries, as soon as possible, not more than 15 calendar days.	Reporting is mandated for ADR observed in post-marketing products including PMS. Reporting period of Serious ADR is within 15 days (or 30 days for expected ADR).	Reporting is mandated for ADR observed in post-marketing products including PMS. SAE : within 15 days from reported day NSAE : within next year Feb from reported day	Reporting is mandated for ADR observed in post-marketing products including PMS. Non serious ADR / Serious but non-life threatening ADR: 15 days from date learned; Serious ADR(fatal and life threatening is within 7days.	Reporting is mandated for ADR observed in post-marketing products including PMS. Reporting period of Serious ADR is within 3-7 days (or on the 30th day of the 1st month of every quarter for expected ADRs).	Fatal/life-threatening ARs: NLT 7 calendar days. Serious ARs: NLT 15 calendar days. Product withdrawal/product recall/product defect: Within 24 hrs Significant safety issues: Within 7 calendar days See The Guidance for Industry – Safety Reporting Requirements for Registered Medicinal Products, April 2011	Reporting is mandated for ADR observed in post-marketing products including PMS. Reporting period of Serious ADR is within 7 days for death and life threatening, within 15 days for other Serious ADR.	Follow Guidance for Industry Post-marketing Safety Reporting Requirements for Human Drug and Biological Products Including Vaccines (Annex 10)
	Variation guideline	Is there any guideline document for post-approval changes? If yes please show the title.	The variations to be approved or filed are listed in Drug Registration Regulation order 28. Meanwhile, Guideline for Variations of Post-market Chemical Drug Products has been implemented.	Please refer to the guidelines for Change of particulars (file name: copGuide).	Chemical products: In case major change, approval is needed within 30 days by submission of variation application. For minor change, it should be notified to the authorities within 30 days. (See Drugs and Cosmetics Rules, 1945) Biological products: LEVEL I - Supplements (Major Quality Changes); LEVEL II - Notifiable Changes (Moderate Quality Changes) LEVEL III - Annual Notification (Minor Quality Changes) (See Guidance for Industry: Post approval changes in Biologic Products – Quality, Safety and Efficacy Documents)	There is regulation number Hk.o3.1.23.12.11.10690 .2011 regarding Implementation of Pharmacovigilance for Pharmaceutical Industry . Variation guideline are included in the Criteria and Procedure of Drug Registration no HK 03/23.10.11.08481. year 2011 /	Partial change application should be submitted for approval of changes. For minor changes, notification system can be applied. Scope and handling of these changes are stipulated in the Pharmaceutical Affairs Law and several notices.	Changes in post-license should be applyed to MFDS according to the level of the changes. Pharmaceutical Affairs Act, Several notices and Guidelines exist.	Malaysian Variation Guideline For Pharmaceutical Products (Date of first edition: 12 April 2013)	Partial change application should be submitted for approval of changes. For minor changes, notification system can be applied. (Pending implementation) See attached files MaV and MiV PFDA has adopted the ASEAN Variation Guidelines for Pharmaceutical Products Final Draft 7.2 2013	There are two sub-categories for each Major and Minor variation. Guidelines are found in Chapter H and Appendix 15 for MIV and Chapter G for MAV.(Updated guideline is effective 1 April 2014). . The Guideline is also guided by the adoption of the ASEAN Variation Guideline.	"drug review and registration guideline" was specify the document needed for post approval change.	Yes, "Asean variation guideline" which will be implemented in Jul 2013. ASEAN Variation Guideline

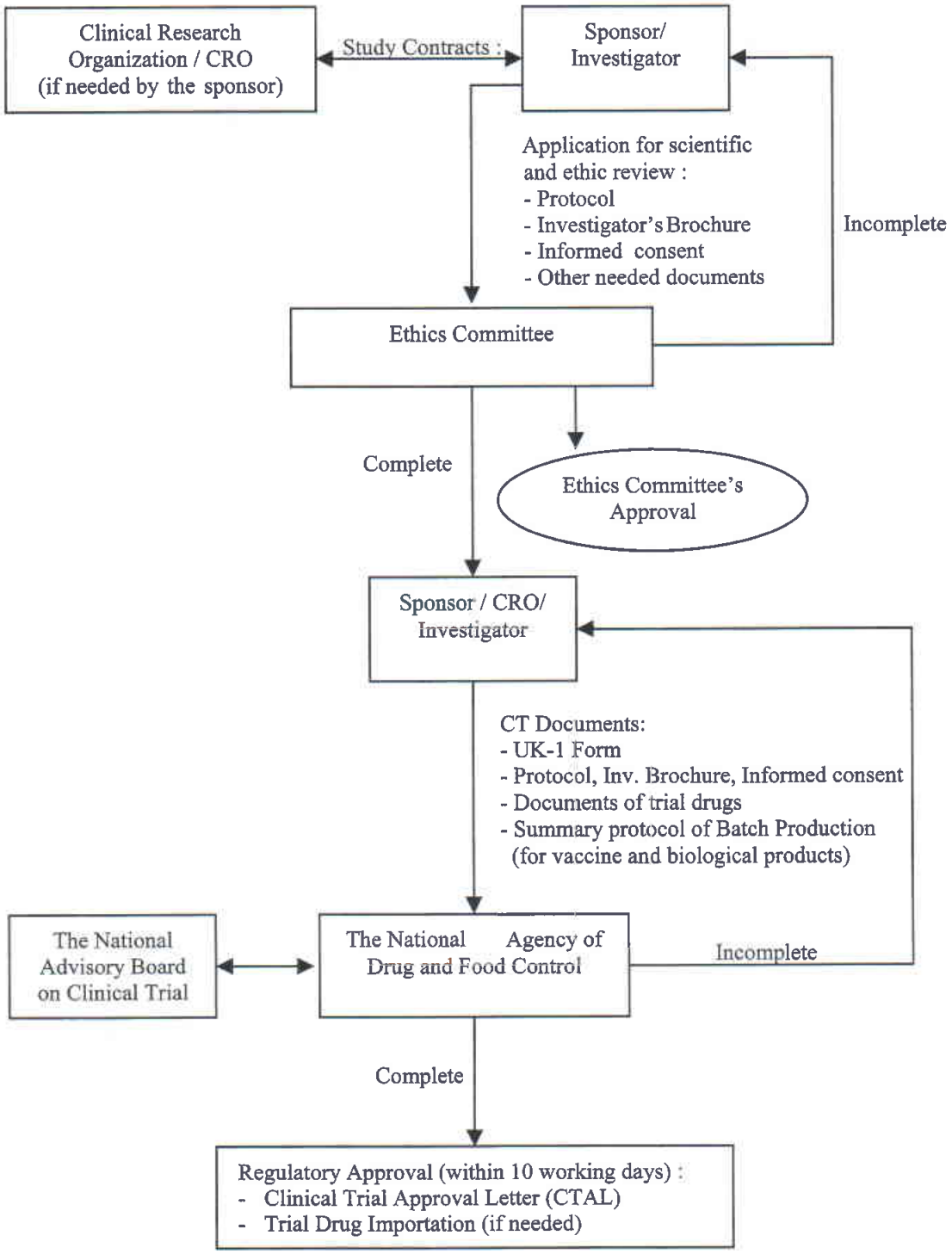
ATTACHMENT IIa
DECREE OF THE HEAD OF THE NATIONAL AGENCY OF DRUG AND FOOD CONTROL
REPUBLIC OF INDONESIA
NO 02002/SK/KBPOM
REGARDING CLINICAL TRIAL PROCEDURE

Flow Chart
Pre-Marketing Trial



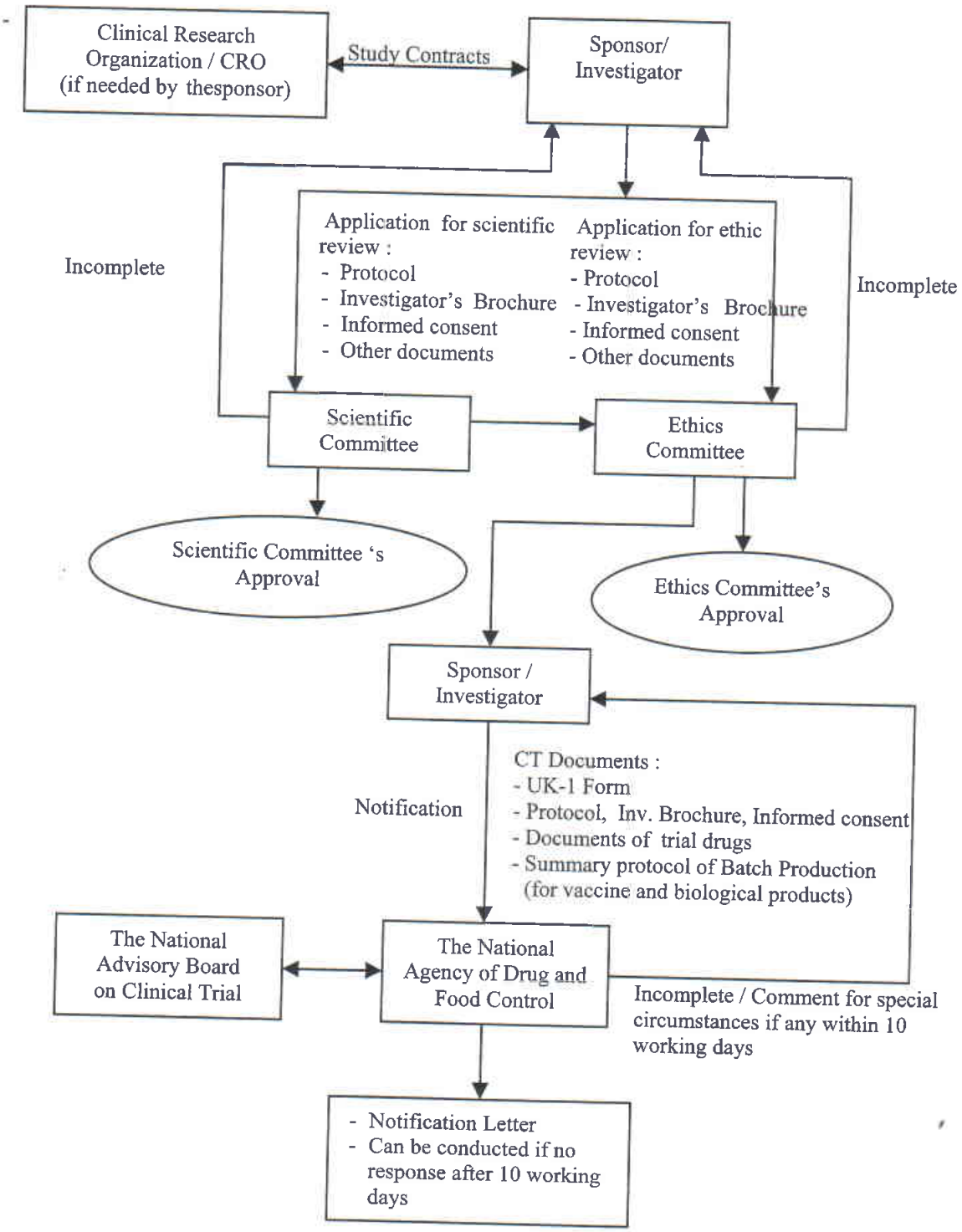
ATTACHMENT IIb
DECREE OF THE HEAD OF THE NATIONAL AGENCY OF DRUG AND FOOD CONTROL
REPUBLIC OF INDONESIA
NO 02002/SK/KBPOM
REGARDING CLINICAL TRIAL PROCEDURE

Flow Chart
Pre-Marketing Trial
(Inseparate Scientific and Ethics Committee)



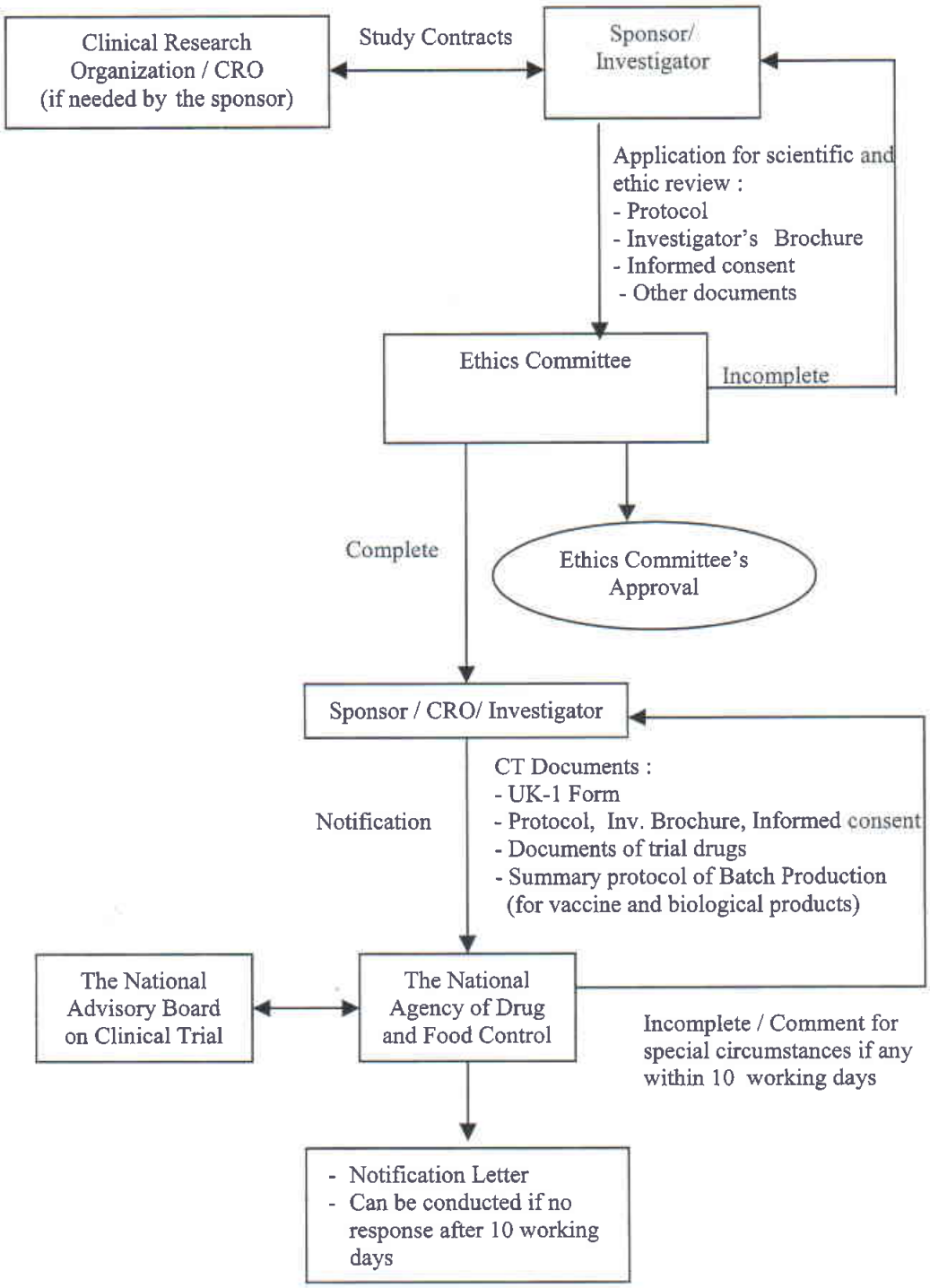
ATTACHMENT IIIa
DECREE OF THE HEAD OF THE NATIONAL AGENCY OF DRUG AND FOOD CONTROL
REPUBLIC OF INDONESIA
NO 02002/SK/KBPOM
REGARDING CLINICAL TRIAL PROCEDURE

Flow Chart
Post-Marketing Trial
(Separate Scientific and Ethics Committee)



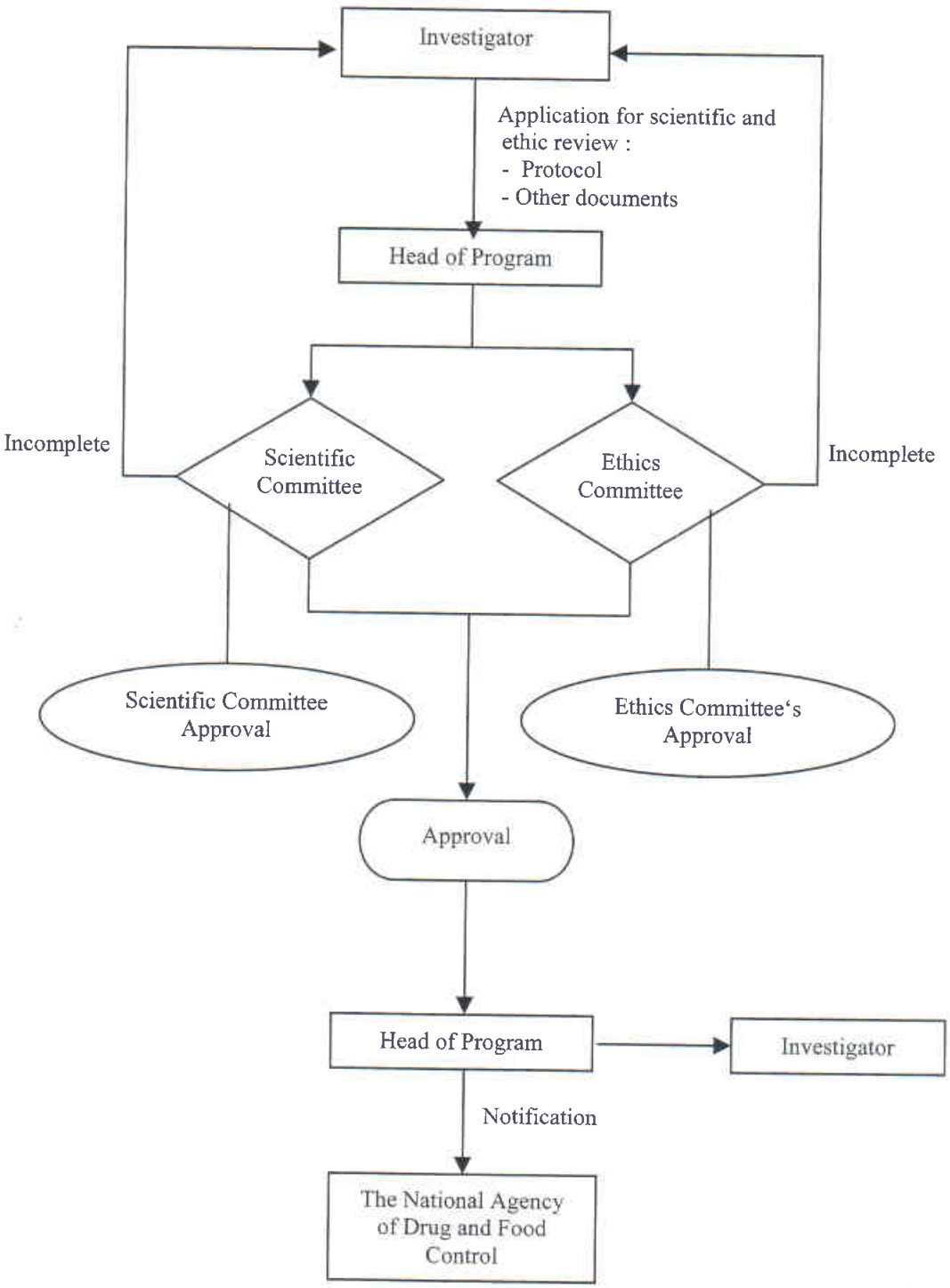
ATTACHMENT IIIb
DECREE OF THE HEAD OF THE NATIONAL AGENCY OF DRUG AND FOOD CONTROL
REPUBLIC OF INDONESIA
NO 02002/SK/KBPOM
REGARDING CLINICAL TRIAL PROCEDURE

Flow Chart
Post-Marketing Trial
(Inseparate Scientific and Ethics Committee)



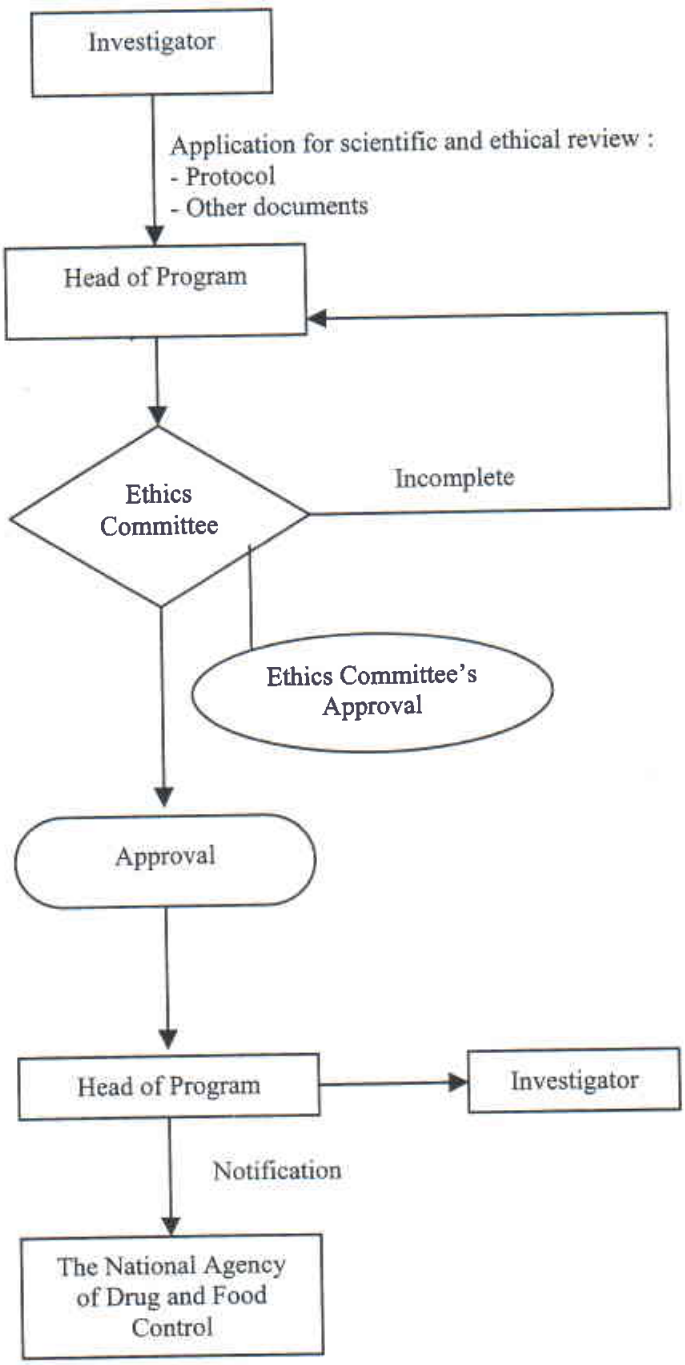
ATTACHMENT IVa
DECREE OF THE HEAD OF THE NATIONAL AGENCY OF DRUG AND FOOD CONTROL
REPUBLIC OF INDONESIA
NO 02002/SK/KBPOM
REGARDING CLINICAL TRIAL PROCEDURE

Flow Chart
Trial for Educational Purpose
(Separate Scientific and Ethics Committee)

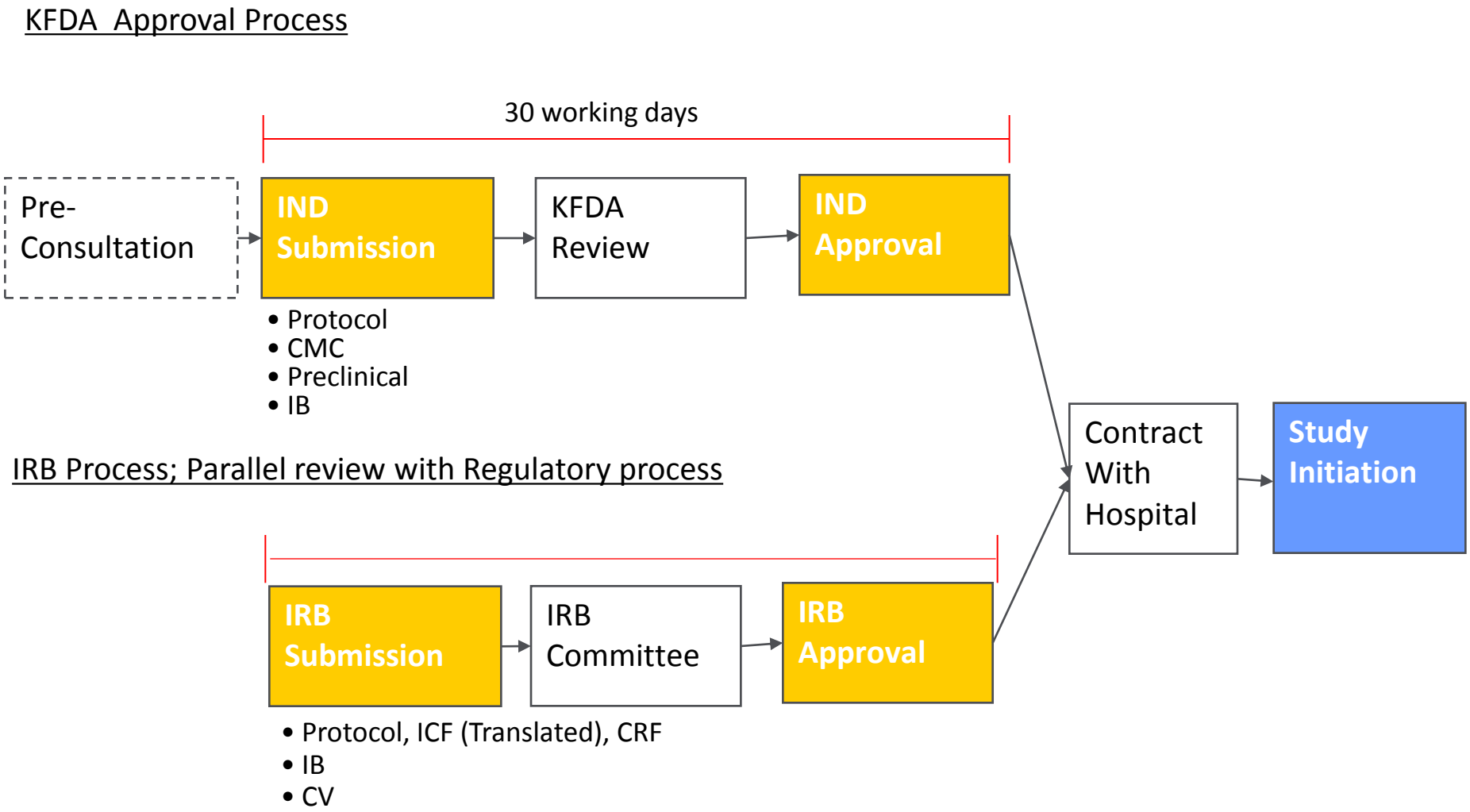


ATTACHMENT IVb
DECREE OF THE HEAD OF THE NATIONAL AGENCY OF DRUG AND FOOD CONTROL
REPUBLIC OF INDONESIA
NO 02002/SK/KBPOM
REGARDING CLINICAL TRIAL PROCEDURE

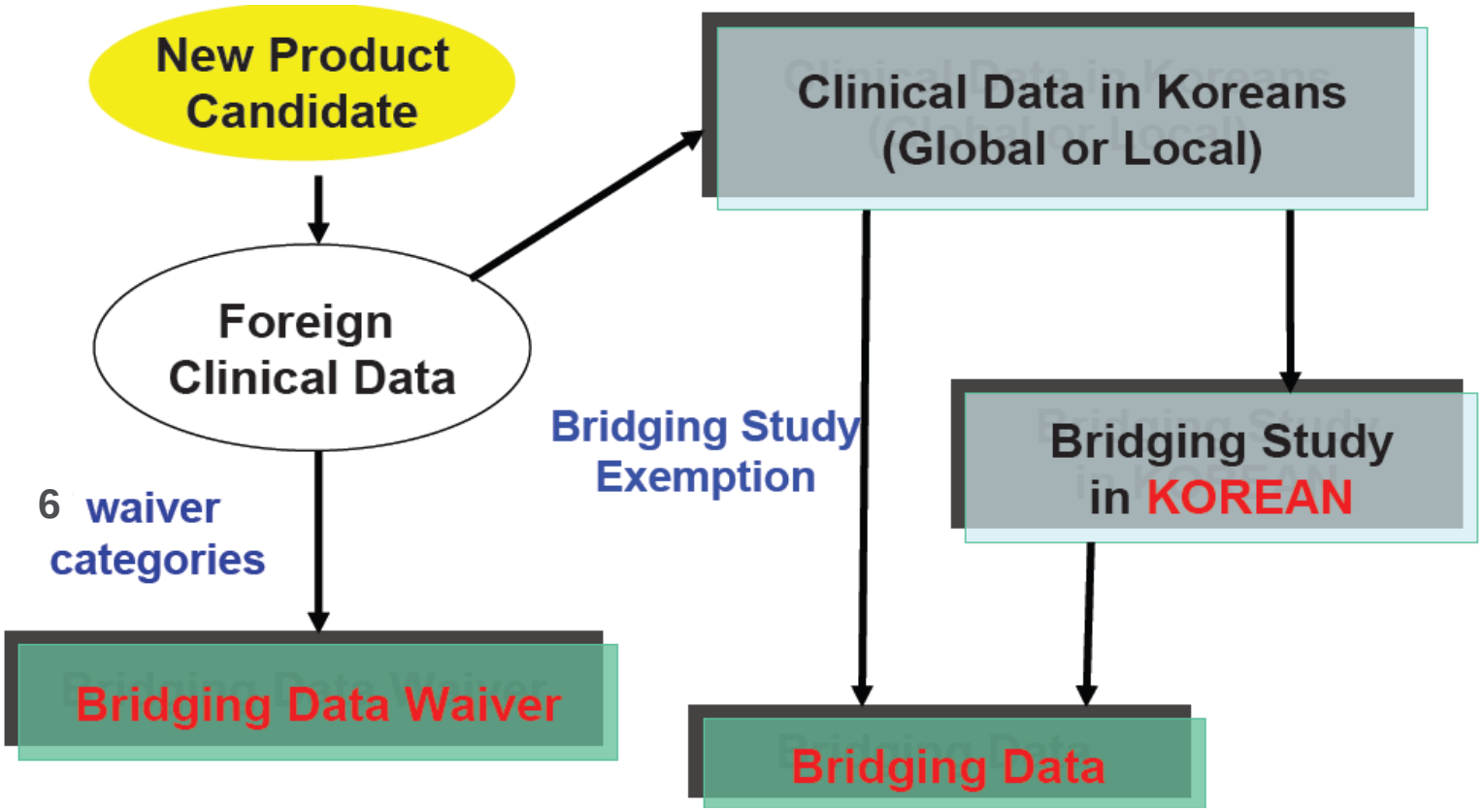
Flow Chart
Trial for Educational Purposes
(Inseparate Scientific and Ethics Committee)



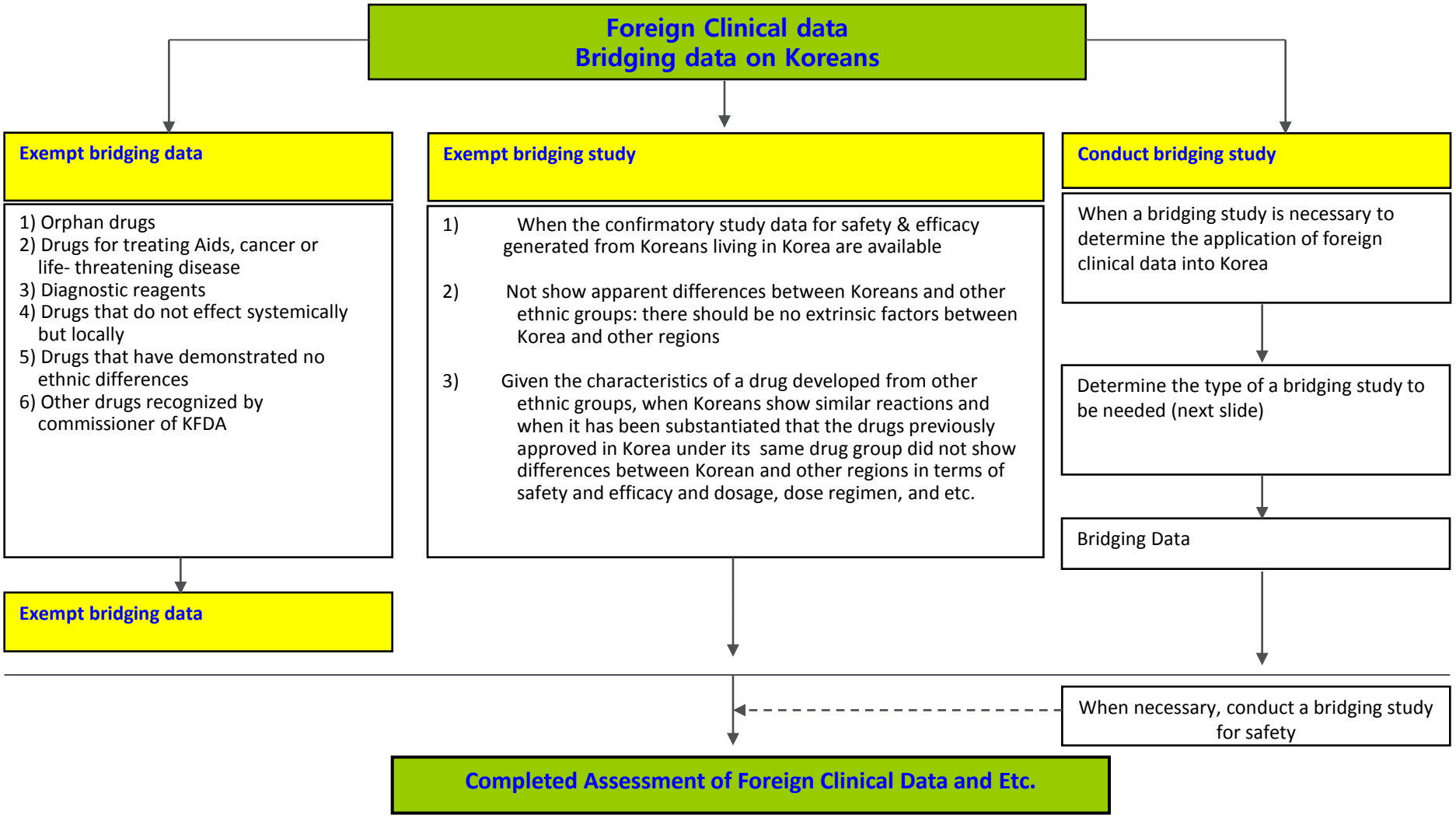
Annex 2


KFDA Approval Process
30 working days
Pre-Consultation
IND Submission
KFDA Review
IND Approval
• Protocol
• CMC
• Preclinical
• IB
IRB Process; Parallel review with Regulatory process
Contract With Hospital
Study Initiation
IRB Submission
IRB Committee
IRB Approval
• Protocol, ICF (Translated), CRF
• IB
• CV

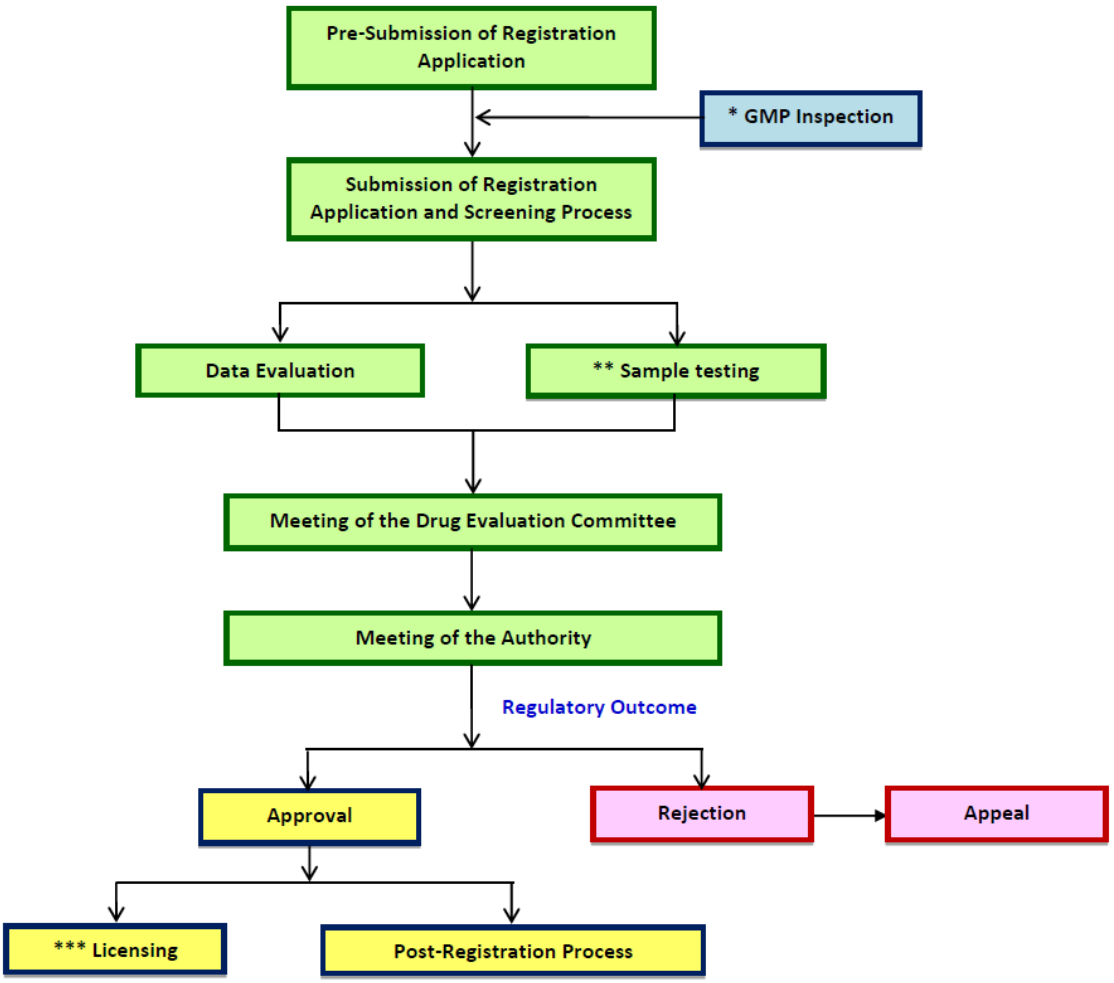
Annex 3


New Product Candidate
Foreign Clinical Data
6 waiver categories
Bridging Data Waiver
Clinical Data in Koreans (Global or Local)
Bridging Study Exemption
Bridging Study in KOREAN
Bridging Data

Annex 3


Foreign Clinical data
Bridging data on Koreans
Exempt bridging data
1) Orphan drugs
2) Drugs for treating Aids, cancer or life- threatening disease
3) Diagnostic reagents
4) Drugs that do not effect systemically but locally
5) Drugs that have demonstrated no ethnic differences
6) Other drugs recognized by commissioner of KFDA
Exempt bridging data
Exempt bridging study
1) When the confirmatory study data for safety & efficacy generated from Koreans living in Korea are available
2) Not show apparent differences between Koreans and other ethnic groups: there should be no extrinsic factors between Korea and other regions
3) Given the characteristics of a drug developed from other ethnic groups, when Koreans show similar reactions and when it has been substantiated that the drugs previously approved in Korea under its same drug group did not show differences between Korean and other regions in terms of safety and efficacy and dosage, dose regimen, and etc.
Conduct bridging study
When a bridging study is necessary to determine the application of foreign clinical data into Korea
Determine the type of a bridging study to be needed (next slide)
Bridging Data
When necessary, conduct a bridging study for safety
Completed Assessment of Foreign Clinical Data and Etc.

Registration process includes quality control, inspection & licensing as well as post-registration process of medicinal products is illustrated in **Figure 2** below:

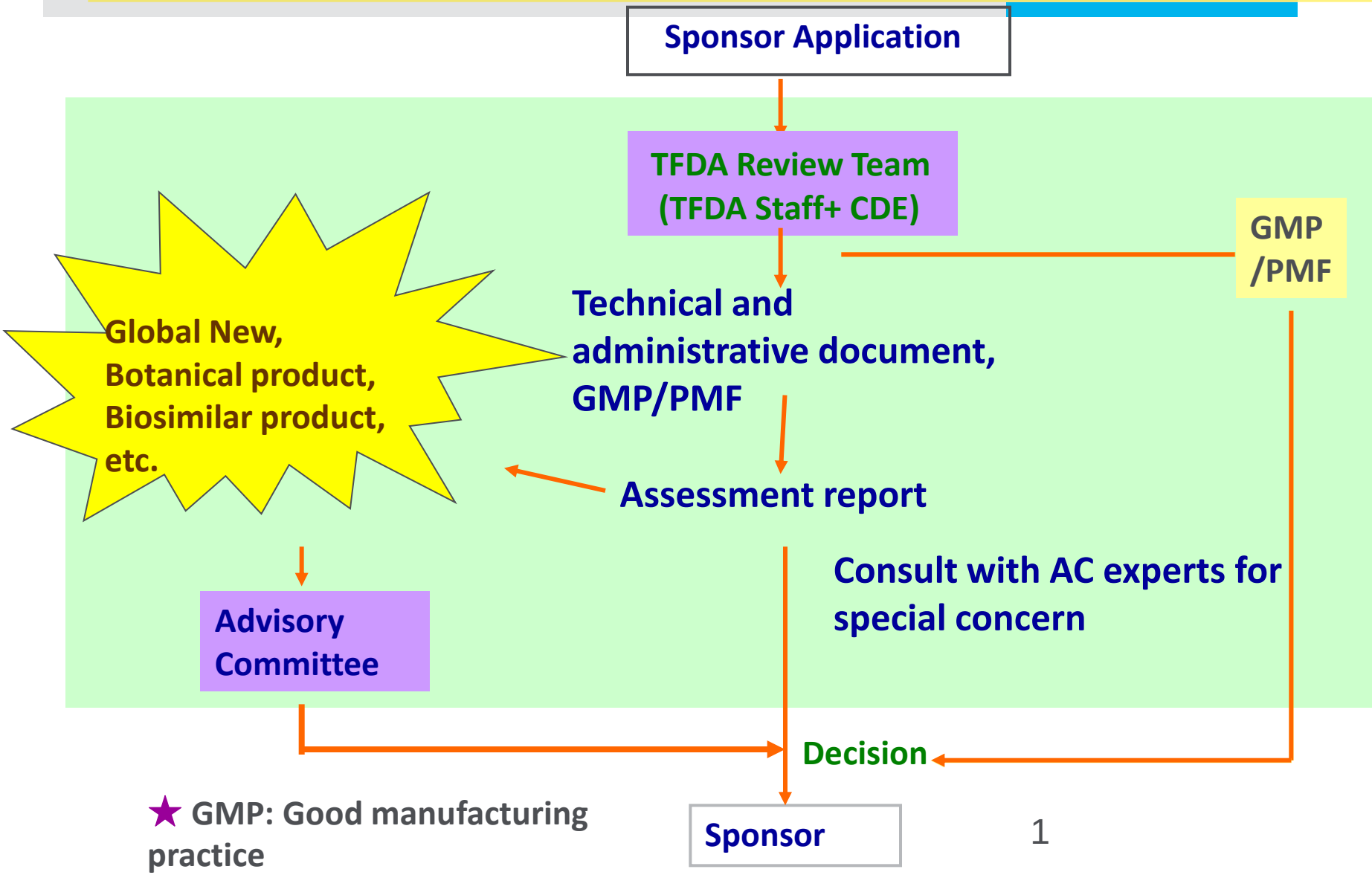


* Good Manufacturing Practice (GMP) Certification

** For natural products only

*** Application for Manufacturer, Import and/or Wholesale License

Review Process for NDA

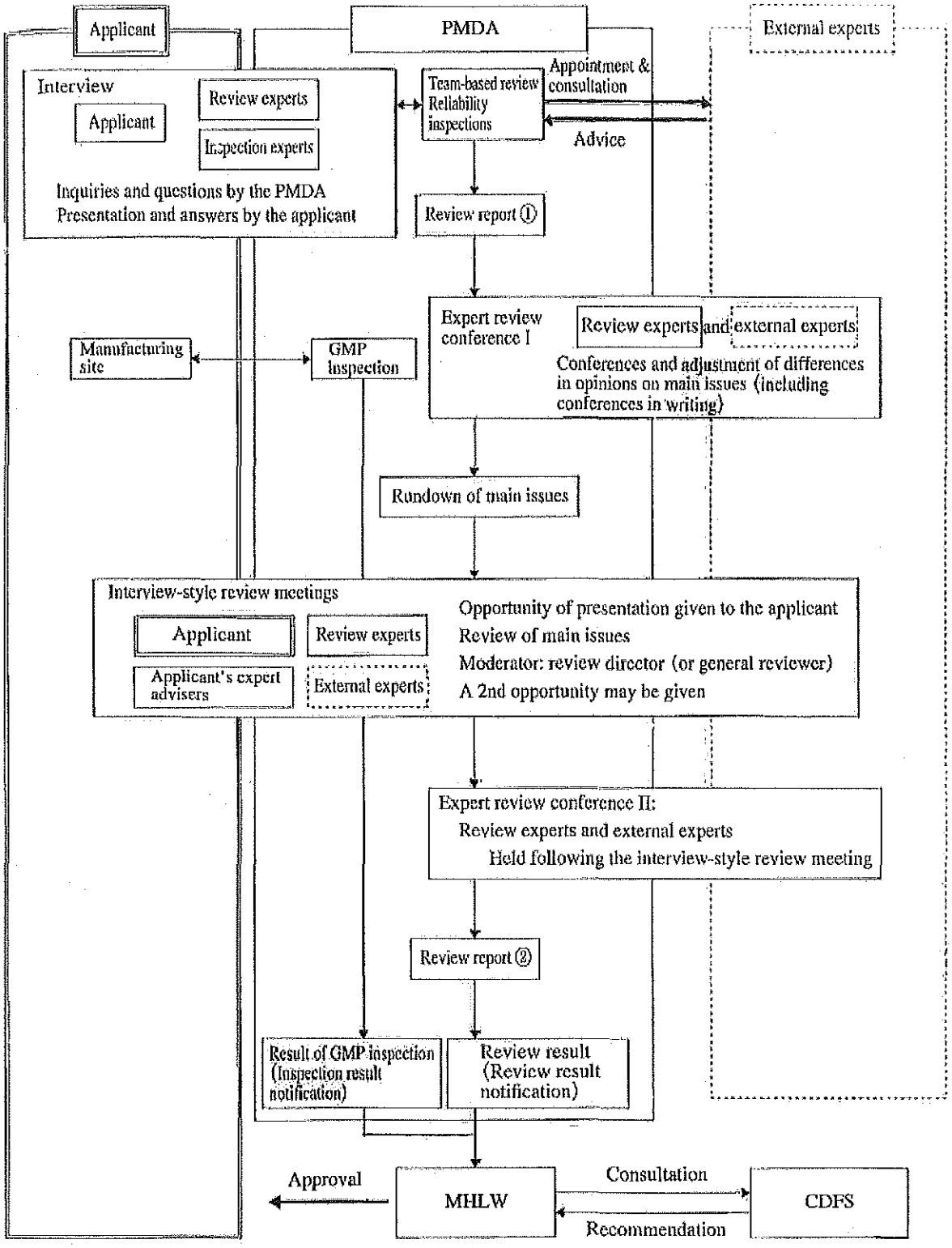


★ GMP: Good manufacturing practice

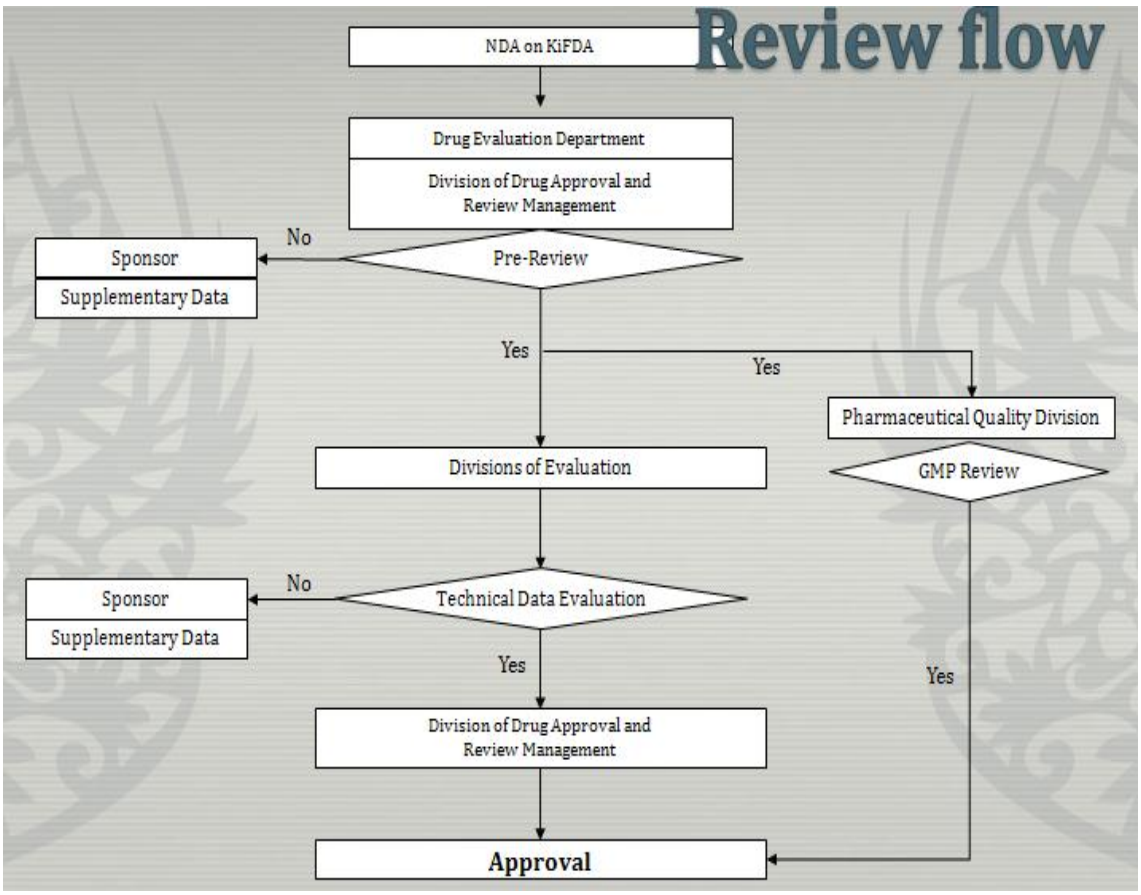
PMF: Plant master file

1

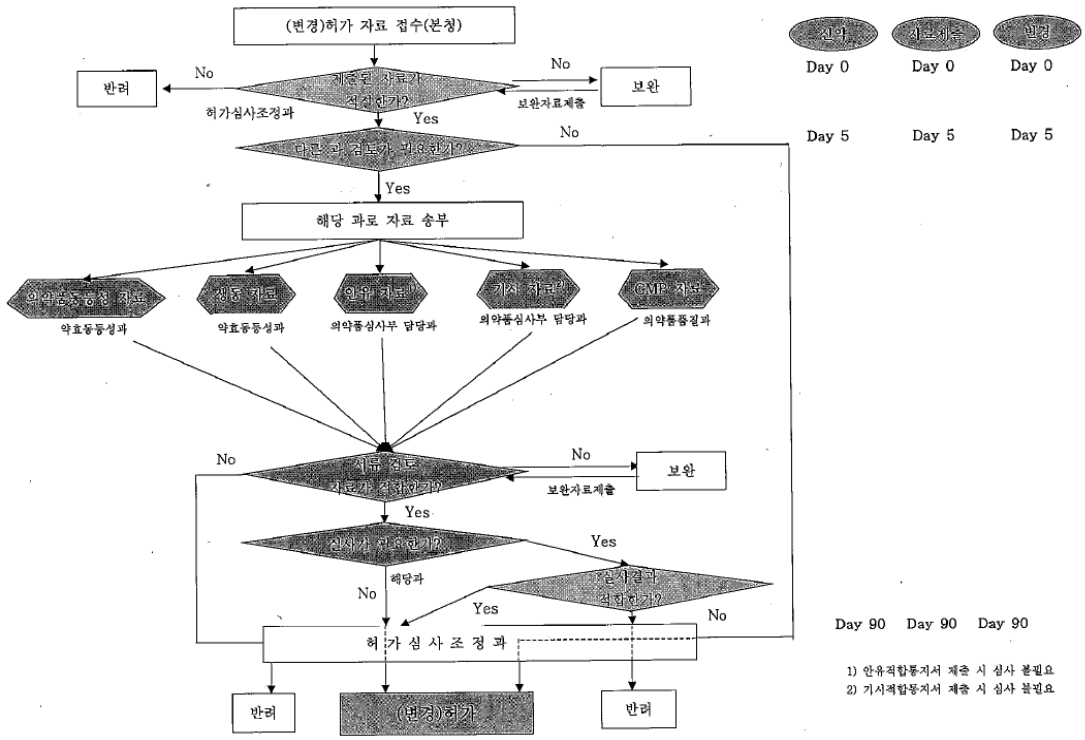
Application Review Process



(Source: Jiho. Drug Approval Licensing Procedures in Japan 2010. Tokyo. Jiho, Inc, 2011; P. 489.)



3. 제조·수입 품목 (변경)허가



Number of reviewers	New Drugs							New Generic (NG)	Generic (G)	Biologics		
	NCE	NI	NCO	ND	NR	NDOS	NS			NB	BF	B
CMC	2	-	2	2	2	2	2	2	2	2	2	2
Clinical	2	2	2	2	2	2	2	2(BA/BE)	-	2	1	
Non-clinical	2	2*	1*	1*	1*	-	1*	(labelling,efficacy&safety	(labelling,efficacy&safety	2	1	1(labelling,efficacy&safety)

* If applicable

NCE = New Chemical Entity,
NI = New Indication,
NCO = New Combination,
ND = New Delivery system,
NR = New Route of administration,
NDOS = New Dosage form of Approved New Drug,
NS = New Strength of Approved New Drug
NB = New Biological drug
BF = New Generic of Biological drug

New Drug Registration
Thailand

REGISTRATION PROCEDURE

Annex 9

FDA Drug Bureau

Step I

Application for Importing of Drug Sample

Submit Application

Permit for Importing Drug Sample

1 days

Step II

Application for Registration

Submit Registration File

Document Checking and Preliminary Review

Experts and/or Subcommittee

Accept

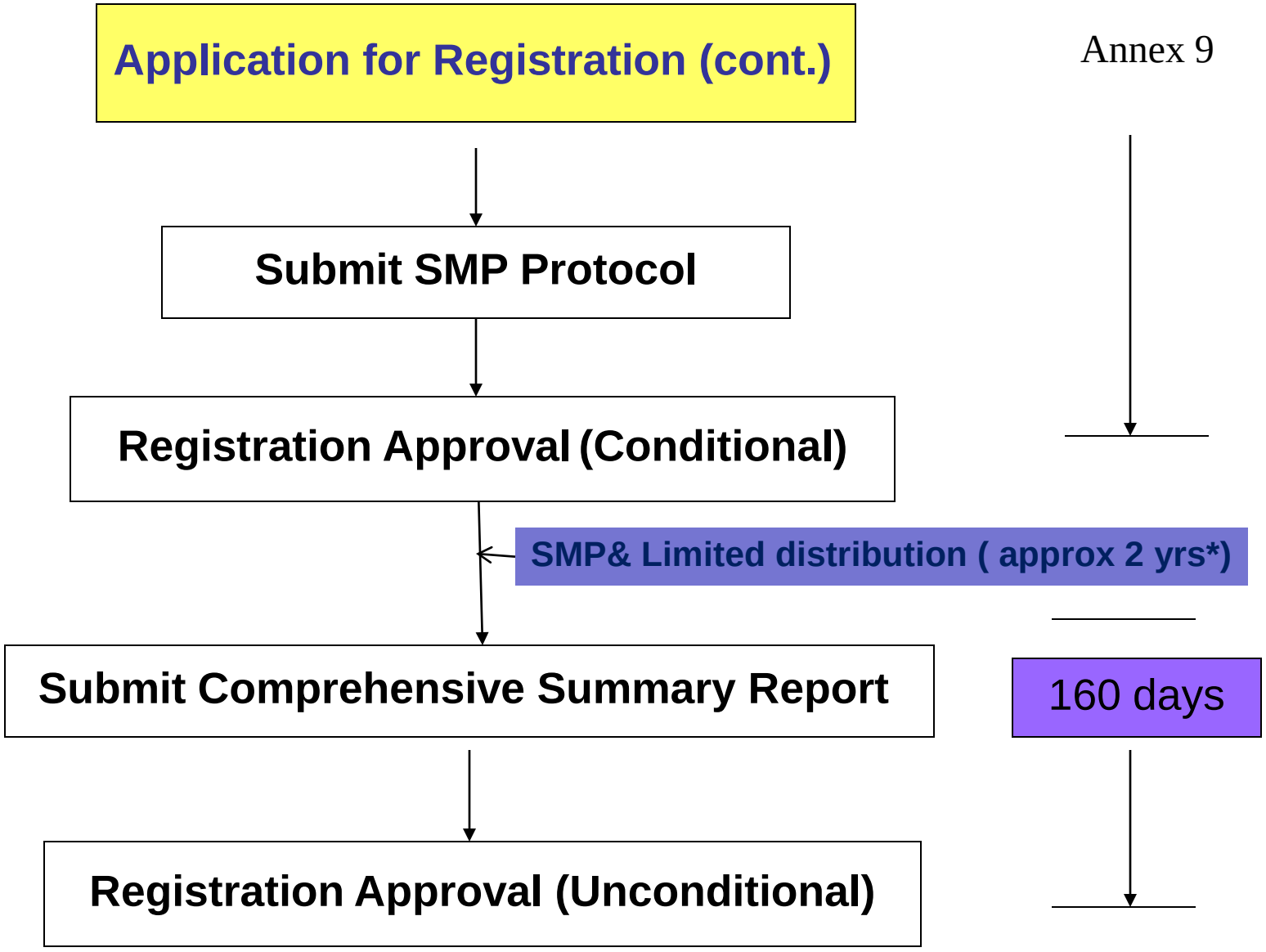
Revise or Request for Add. Document

Review

Accept

280 wd

Annex 9



Note: *Time can be extended from 2 years up to 4 years if justified

Guidance for Industry

Post-marketing Safety Reporting Requirements for Human Drug and Biological Products Including Vaccines

Food and Drug Administration

13 July 2011

Table of Contents

Guidance for Industry

Post-marketing Safety Reporting Requirements for

Human Drug and Biological Products Including Vaccines

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 reactions following the marketing of a drug is crucial to pharmacovigilance. The Thai FDA has put in place a requirement upon registration of a new drug: that market authorization holders (MAHs) have to report adverse reactions/ events as a condition for a conditional approval. Subsequently, the Thai FDA also imposed a requirement for such reporting for all vaccines and has received good cooperation.

To improve effectiveness and standardize the pharmacovigilance requirements, the Thai FDA, representing by the Health Product Vigilance Center (HPVC), in cooperation with the Pharmaceutical Research and Manufacturers Association (PReMA) has issued the guidance document. This document serves as a guide for MAHs to implement pharmacovigilance activities after a drug is marketed. This guidance covers purpose and scope, individual case safety reports, reporting requirements in special situations, reporting flow charts, glossary, and reporting forms.

2. Purpose and Scope

The purpose of this document is to guide Marketing Authorization Holders (MAHs) on the submission of relevant safety information to Health Product Vigilance Center (HPVC) of the Food and Drug Administration, Ministry of Public Health. However, this guidance does not include medicinal products which are imported under the remit of the Bureau of Drug Control, the Thai FDA, for clinical studies.

This guidance consists of the following topics:

- Reporting requirements for individual case safety report
- Spontaneous or unsolicited AE report
- Scientific literature report
- Reporting requirements in special situations
- Solicited report

- Periodic Safety Update Report (PSUR)

3. Reporting Requirements for Individual Case Safety Reports (ICSRs)

The MAH should report AEs of registered drugs and biological products Including vaccines that are spontaneously received to HPVC. Only serious suspected AEs should be reported to HPVC according to the process and time frame shown in Annex 1.

3.1 Essential Information in AE Reports

AE reports should be as complete as possible and contain essential information to facilitate assessment.

The minimum information required for submission of an initial AE report is:

1. An identifiable patient
2. An identifiable reporting source
3. At least one adverse event
4. At least one suspected product

3.2 Follow-up Reports

Additional information should be provided in the form of follow-up reports which should be clearly stated as such with reference to the initial report.

3.3 Expedited Reporting

Upon the first knowledge of a fatal adverse event associated with use of a vaccine or a new drug with conditional approval (NC), or death from unexpected/unlabelled ADRs, the MAH should notify the FDA by phone, fax within 24 hours and send a complete report within 7 calendar days of the first knowledge.

3.4 AE Reporting Channels

(1) the online reporting system which is available at:
http://www.fda.moph.go.th/vigilance (passwords required)

(2) the Thai FDA AE reporting form with or without the CIOMS I form, and submit the reports via fax, email, mail to HPVC.

(3) The Thai FDA AE reporting form can be downloaded from:

http://www.fda.moph.go.th/vigilance/

The CIOMS I form is available at: http://www.cioms.ch/

3.5 Time Frames for Reporting

The time frame depends on type of AE reports. Please see the table below:

Adverse Events	Reporting Time Frame
Death	As soon as possible but not later than 7 calendar days, except the following circumstances whereby the FDA should be notified by phone, fax, email within 24 hours, followed by a complete report within 7 days of the first knowledge: (1). Death after use of • Vaccine • New drug with conditional approval (NC) (2) Death from unexpected/unlabelled ADRs
Serious	15 calendar days*
Non-serious	2 months

*****Calendar Day from the MAH's receipt date of the report.

4. Spontaneous or Unsolicited AE Reports

4.1 Serious Adverse Events

Only serious adverse event reports that are suspected to be associated with drugs, biological products or vaccines should be submitted.

4.2 Non-Serious Adverse Events

(1) Non-serious AE reports, originated in Thailand, for all vaccines and for drugs and biological products under conditional approval should be submitted.

(2) Other such reports, originated in Thailand, should not be submitted, except upon request by the Thai FDA.

(3) AE reports originated in foreign countries should not be submitted except that the AE involves a product purchased from Thailand or occurs to a Thai citizen.

5. Scientific Literature Reports

Cases of AEs reported in scientific and medical literature, including relevant published abstracts from meetings, may qualify for reporting if the source country is Thailand, the minimum information for reporting (see 3.1) is met, and the AEs are serious. The publication reference (s) should be given as the report source.

If multiple products are mentioned in the article, a report should be submitted only by the applicant whose product is suspected. The suspected product is identified as such by the article's author.

6. Safety Reporting in Special Situations

6.1 Lack of Efficacy

Synonyms: lack of effect, failure of expected pharmacological actions, etc.

Lack of efficacy 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.

6.2 Exposure During Pregnancy

In the event that a MAH is aware that its product which is not recommended for use during pregnancy has been received by a pregnant patient, the MAH should follow up with the doctor on the pregnancy outcome. If a pregnancy results in a serious or an abnormal outcome which the reporting doctor considers might be due to the product, the MAH must submit the AE report to the HPVC within 15 calendar days.

6.3 Drug Overdoses

The MAH does not need to report cases of drug overdoses unless these lead to adverse events.

7. Solicited Reports

Solicited AE reports derived from organized data collection systems including studies e.g. phase IV clinical studies, may qualify for reporting to HPVC if the following is fulfilled:

(1) The medicinal product is used according to the approved label and prescribing information, and
(2) The medicinal product used in the study does not require an import permit from the Bureau of Drug Control
(3) Only serious adverse events from such studies need to be submitted.

8. Periodic Safety Update Reports (PSURs)

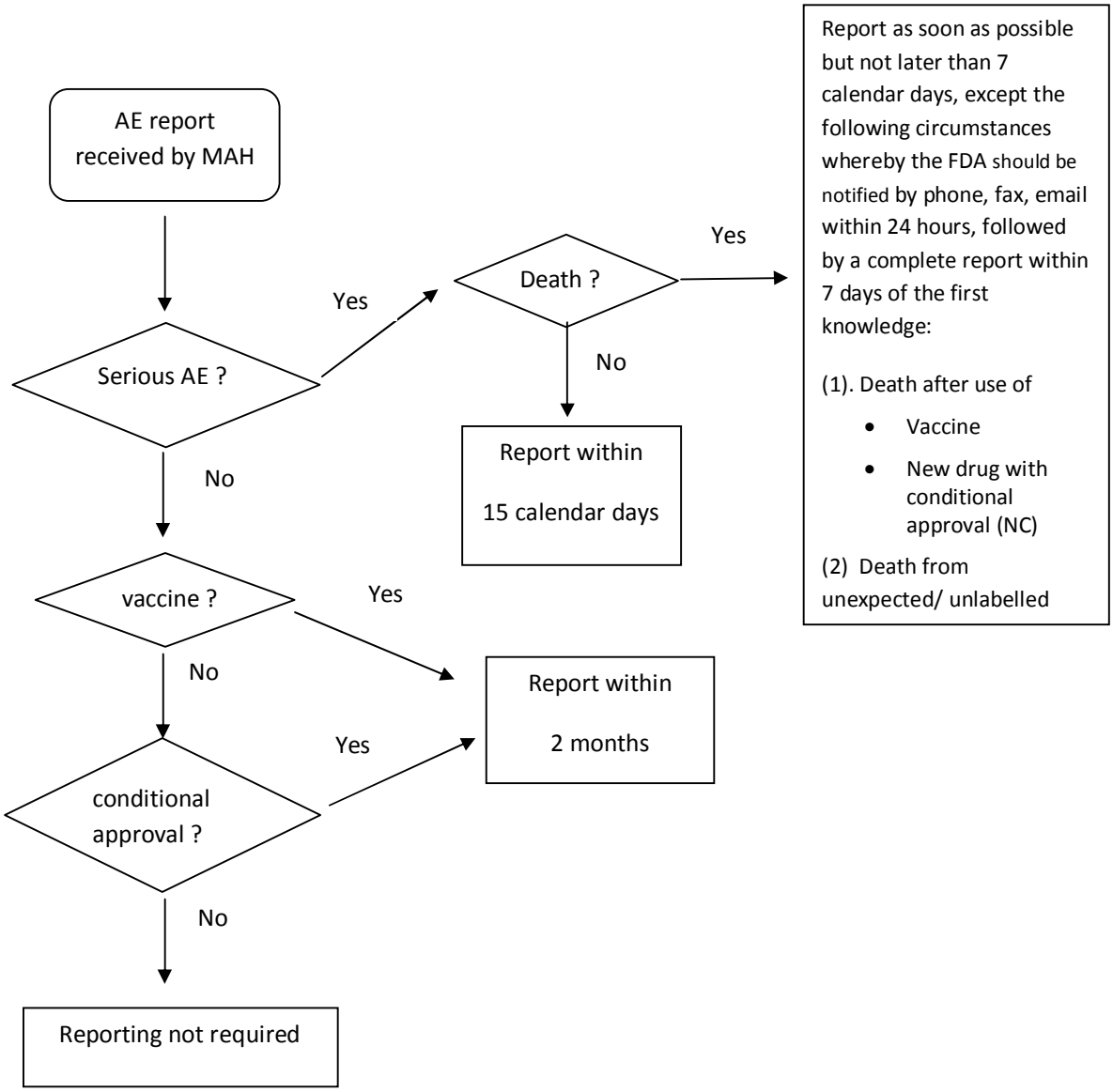
MAHs are not required to submit PSURs except when requested by the Thai FDA.

9. Other Safety Information

When the MAH receives product safety information which may warrant changes in risk management measures, the MAH should send the information to HPVC as soon as possible.

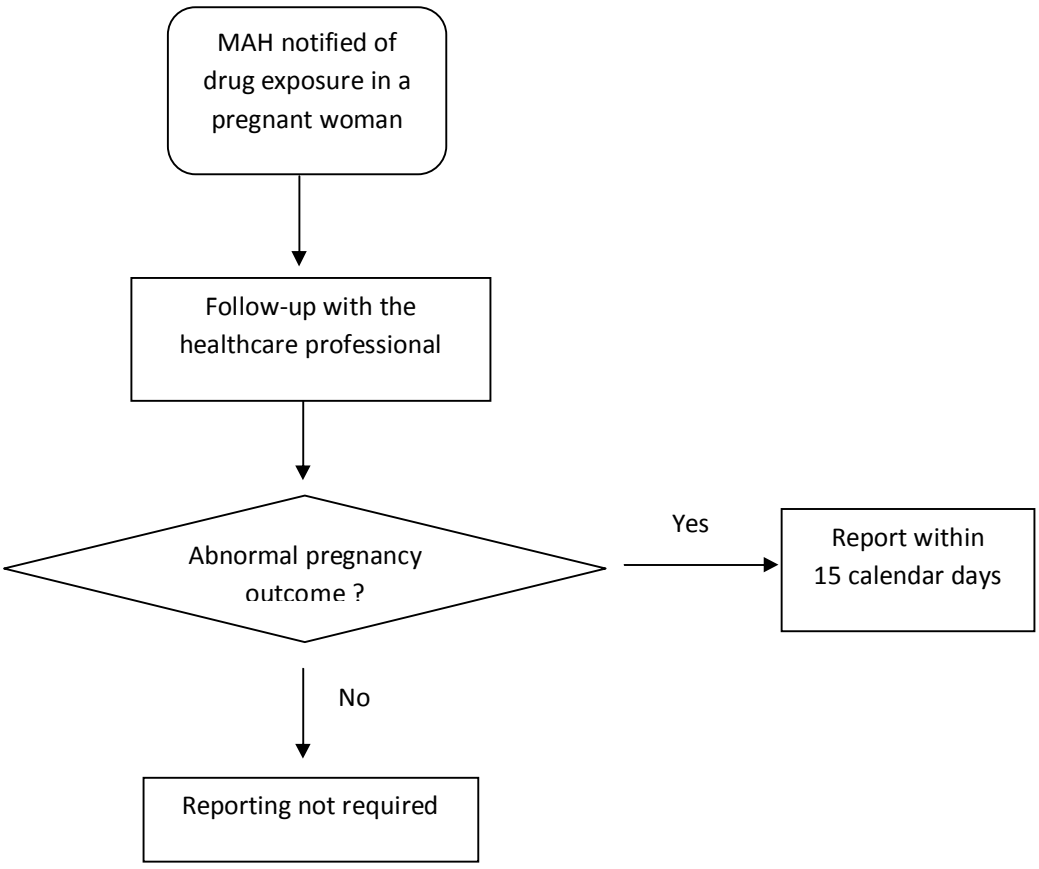
Annex I

Flow Chart A: Post-Marketing Adverse Event Reporting to HPVC



Annex I

Flow Chart B: Reporting of Drug Exposure During Pregnancy to HPVC



Annex II

The Thai FDA AE Reporting Form in Thai (See the HPVC website)

Annex III CIOMS FORM

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. 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-
17. INDICATION(S) FOR USE		DUCTION? ☐ YES ☐ NO ☐ NA
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 ADRESS 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 IV : Glossary

Adverse event or Adverse Experience (AE:

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.

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.

Causality assessment:

Causality assessment is the systemic review of data about an adverse reaction case to determine the likelihood of a causal association between the event and the medicinal product received.

CIOMS I form:

An adverse reaction 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.

Labelled/ Unlabelled adverse reaction

An adverse reaction, the nature or severity of which is/is not consistent with domestic labeling or market authorization.

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.

Serious AE :

A serious adverse event is any untoward medical occurrence that at any dose:

- 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,
- is a medically important event or reaction.

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.

Marketing Authorization (MA) :

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

Marketing Authorization Holder (MAH):

The company named on the Marketing Authorization for manufacturing in or importing into the Kingdom of Thailand

Solicited reports

Solicited reports are those derived from organized data collection systems, which include clinical trials, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare providers, or information gathering on efficacy or patient compliance. Adverse event reports obtained from any of these should not be considered spontaneous.

Safety Monitoring Program (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 AEs 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 event 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".

Spontaneous or unsolicited report:

Any unsolicited communication by healthcare professionals or consumers to a company, 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.