VETERINARY DRUG REGISTRATION IN THAILAND

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Veterinary Drug Subgroup
Pre-marketing Control
Bureau of Drug Control
Thai Food and Drug Administration

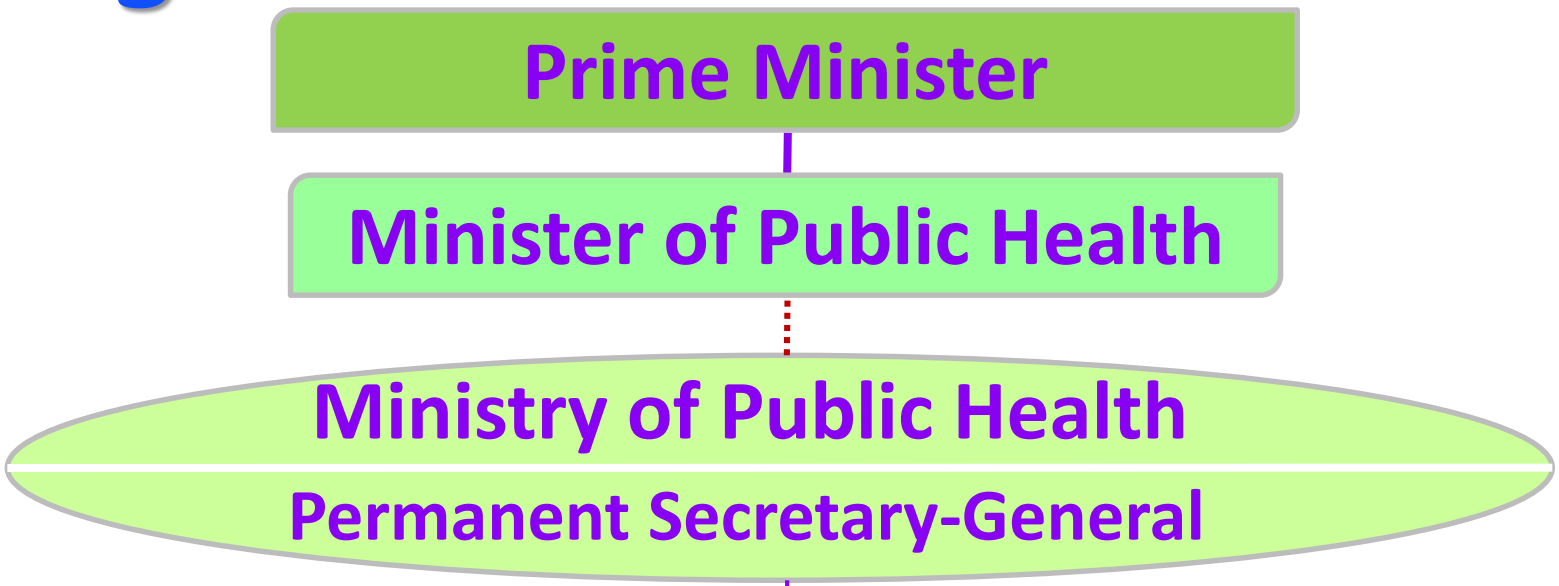
TOPICS

- Organization chart of ThaiFDA, Bureau of Drug Control
- Law : Drug Act
- Definition of Drug
- Drug classification
- Veterinary Drug Registration Process & Documents
- Veterinary Drug Variation
- Banned Veterinary Drugs

Food and Drug Administration

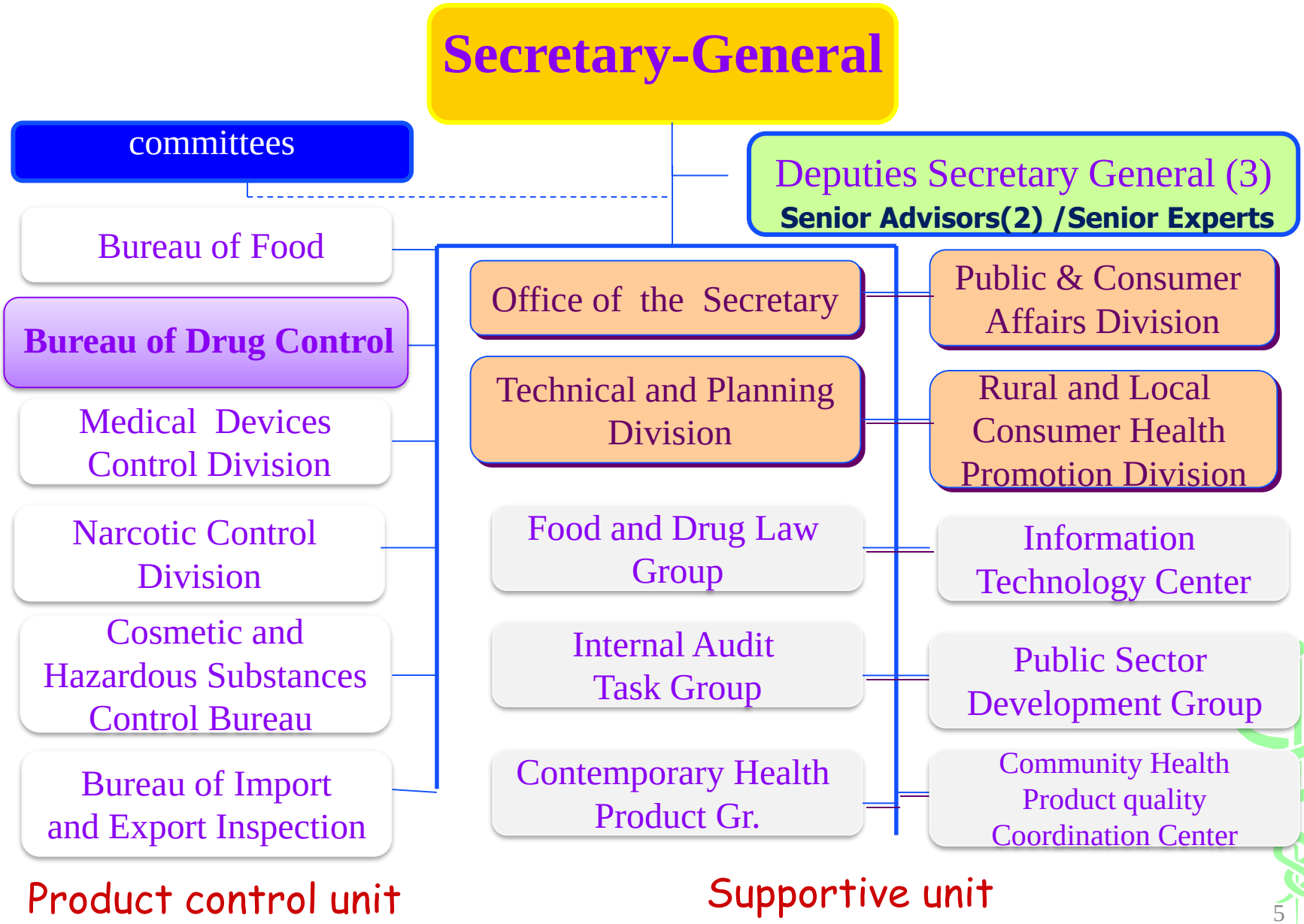
FDA under the supervision of the MOPH

Organization chart of MOPH



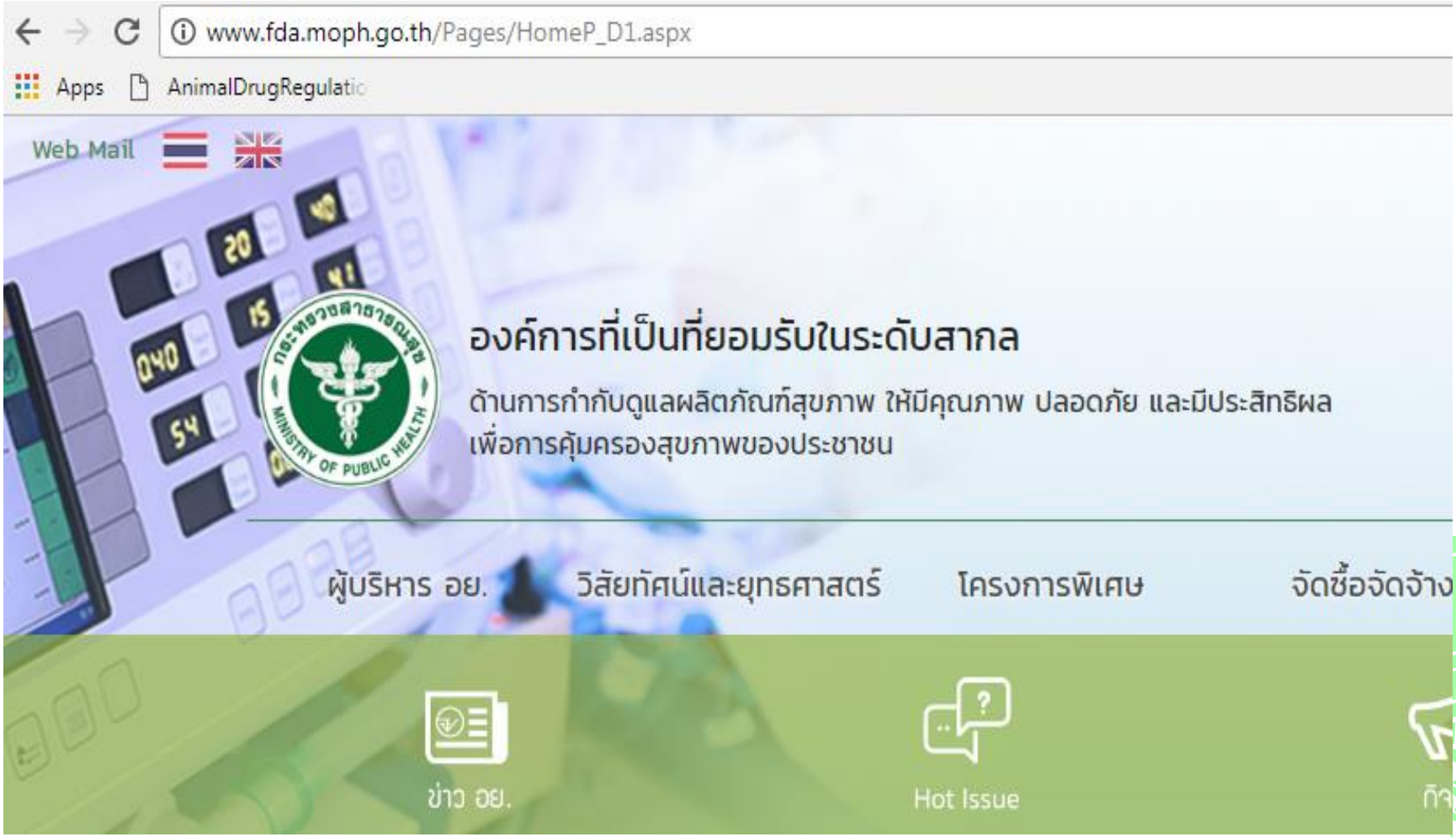
Cluster of **Medical Services Development**	Cluster of **Public Health Services Support**	Cluster of **Public Health Development**
• Dept of Medical Services • Dept of Mental Health • Dept of Thai Traditional and Alternative Medicine Development	• Dept of Medical Science • Dept of Health Services Support • **Thai FDA**	• Dept of Disease Control • Dept of Health

Organization chart of Thai FDA



Website

http://www.fda.moph.go.th/Pages/HomeP_D1.aspx



Structure of Bureau of Drug control

- Section of General Administration
- Division of System Development
- Division of Standards and Regulation
- Division of Pre-Marketing Control
- Division of Post-Marketing Control
- Division of National Drug Policy
- Division of Traditional & Herbal Drug

- Pre-marketing control
  - Chemical Drug Section
  - Veterinary Drug Section
  - Biological Product Section
  - Investigational New Drug (IND) Section
  - Advertising Control Section

Drug LAW

"Drug Act, B.E. 2510 (1967) and its four amendments"

- Drug Act (No.2) B.E. 2518 (1975)
- Drug Act (No.3) B.E. 2522 (1979)
- Drug Act (No.4) B.E. 2527 (1984)
- Drug Act (No.5) B.E. 2530 (1987)

Responsibility Areas, under Drug Act

- licensing the production, importation and sale of drugs in Thailand;
- ensuring that drug products available to consumers are of standard quality, efficacy and safety; and
- controlling and monitoring both pre and post-marketing phases of manufacture, import, transport, storage and sale.

Drug Act - Main activities

- Pre-marketing & Post-marketing Control
- Surveillance program on Product Safety
- Surveillance system on Advertisement
- International Affairs regarding P'cals/Biological
- Data-base on Registered Pharmaceuticals
- Cooperation with other Agencies

Marketing Authorization

Licensing activity

Post Marketing Surveillance

Safety Monitoring Programme-SMP

Advertisement Controlling

IND-Clinical Trial Authorization

ASEAN, APEC, Global/WHO Cooperation Forum/Program

FTA & TRIPs forum

Etc……

DRUG is defined as (section 4)

" Substances recognized by pharmacopoeias notified by the Minister"

"Substances intended for use in the diagnosis, treatment, relief, cure or prevention of human or animal disease or illness".

-Substances which are pharmaceutical chemicals or semi processed pharmaceutical chemicals"

"Substances intended to affect the health, structure or function of that human or animal body".

Drugs not including

Drugs shall not include substances :

- intended for use in agriculture or industry as notified by the Minister
- intended for use as food for human, operating goods, medical apparatus, cosmetics or device for use in the practice of medicine and a component
- intended for use in science laboratory for research, analysis or verification of disease which is not directly done to human body

MINISTERIAL REGULATION ON
substances which are exempt from being classified as drug
No. 34 B.E. 2560 (2017)

- Medicated premix classified as drug, controlled by FDA
- Medicated feed is exempt from being classified as drug, therefore
  - Medicated feed is regulated by DLD
  - Only registered drug products can be used in medicated feed.

Official Pharmacopoeias
(modern drugs) notified by the Minister

- USP 34th rev., NF 29th ed. & suppl.
- BP 2011 vol. 1-5 & addenda
- IP 4th ed. & suppl.
- Ph. Eur.7th ed. & suppl.
- Thai Pharmacopoeia II, vol. I part1 & suppl.
- Thai Herbal Pharmacopoeia vol.II, III, & suppl.

Pre-Marketing : Licensing

The drug Act requires that persons who wish to sell, produce, or import drugs into Thailand have to obtain a license from the FDA.

- License to manufacture modern/traditional medicines
- License to sell modern/traditional medicines
- License to import modern/traditional medicines

Pre-Marketing : Registration

- Registration process is necessary to ensure quality, safety and effectiveness of the drugs to be marketed in Thailand.
- Licensed persons who wish to produce or import drugs into Thailand have to apply for registration of drugs before the drugs are produced or imported.
- Only authorized licensees are allowed to apply for drug registration certificates.

Drug Category

- Two main drug categories:
  - Modern drugs for human & animals
    - Chemical drugs
    - Biological drugs
  - Traditional/Herbal drugs for human & animals

TYPE OF MODERN DRUG REGISTRATION

- Chemical drug registration for human & animals
  - Generic Drugs
  - New Drugs
- Biological drug registration for human & animals

Classification of Veterinary Drugs
(Chemical drugs)

- Generic Drugs (Existing drugs)
  - For food producing animals
  - For companion animals
- New Drugs
  - For food producing animals
  - For companion animals

New Drugs

- New Chemical Entities
- New combination
- New delivery system
- New indication
- New strength
- New dosage form
- New species

Veterinary Drug Registration

- Drug Products are proved to be safe, effective, good quality
- The credential registration certificate will be granted
- Drug products can be lawfully marketed
- The granted registration certificate is valid when the license is valid
- The certificate will be automatically expired if the product is not manufactured/imported for 2 consecutive years

Veterinary Drug Registration

Applicants : Only authorized licensees are qualified to apply for product registration

- Licensed manufacturers
  - Local plants: GMP PIC/S compliance
- Licensed importers
  - Overseas plants are required for GMP clearance process

Veterinary Drug Registration Process

- **Step I**

  Apply for permission to manufacture or import of a drug sample for registration

- **Step II (For Importers)**

  Apply for GMP clearance/GMP Certificate for overseas manufacturers

- **Step III**

  Apply for registration certificate approval

VETERINARY DRUG REGISTRATION PROCESS

Step I Apply for permission to manufacture or import of a drug sample for registration

Submit an application

- Application form Nor yor 8/Por yor 8
- Labels/Packaging Inserts

↓

Screening/Review — 1 day (OSSC)

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Approve | **Reject**

Step I : Apply for the permission to manufacture or import of drug samples for registration

- Submit an application form Nor yor 8/Por yor 8
- Label and Leaflet

VETERINARY DRUG REGISTRATION PROCESS

Step II : Apply for GMP Clearance/GMP certificate for overseas Manufacturers (Importers)

Submit an application

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Screening/Preliminary Review

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Scientific Review by Internal Reviewers

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Approve Revise Reject

VETERINARY DRUG REGISTRATION PROCESS

Step II : Apply for GMP Clearance/GMP certificate for overseas Manufacturers (Importers)

- ThaiFDA is a PIC/S member and local manufacturers comply with GMP PIC/S.
- Ensure that the overseas manufacturer complies with GMP PIC/S or equivalent international standards.
- Sponsors are required to obtain GMP clearance/GMP certificate for overseas manufacturers.

VETERINARY DRUG REGISTRATION PROCESS

Step II : Apply for GMP Clearance/GMP certificate for overseas Manufacturers (only importation)

- GMP clearance – document review

Overseas manufacturers are required to support evidence to demonstrate that the manufacturing site is acceptable.

- GMP certificate – on-site inspection

VETERINARY DRUG REGISTRATION PROCESS

Thai FDA applied for PIC/S membership in March 2015 (20 March 2016). A paper assessment was conducted in view of its accession to PIC/S, followed by an on-site assessment provided by PIC/S assessment team on 14 – 18 March 2016. The PIC/S assessment of Thai FDA covered both traditional and modern medicines.

Finally, the PIC/S Committee invited Thai FDA to join the Scheme as PIC/S' 49th Participating Authority from August 1, 2016.

VETERINARY DRUG REGISTRATION PROCESS

StepIII Apply for registration certificate approval

Applicants –Dossier Submission

Completeness review

Screening/Preliminary Review

1/3 days

Technical review

Scientific Review by TFDA/Experts/Subcommittee/Committee

120/160/220 days

Part I Registration form Tor Yor 1

- Packaging Component
- Package leaflet
- Free Sales Certificate
- Sample
- Document support safety and efficacy

Part II

Drug quality and analytical method

- Chemical Document

+ Add. Document/References

Making decision by ThaiFDA

Approve Revise Reject

Experts

- ThaiFDA
- Educational Institutions
- Department of Medical Sciences (under MOPH)
- Health Care Institutions

Step III : Application Dossier/Documents

Part I : Administrative Data and Product Information

- Submit Application form "Yor 1"

Part II : Quality Document

- Submit the drug quality and analytical control method

Part I : Administrative Data and Product Information

- Application form "Yor 1" including product information
  - Dosage form/ Appearance/ Formula - Manufacturing sites
  - Packaging components
- The approval from step I (drug sample permit)
- Certifications
  - CFS (imported drug)
  - GMP Clearance/GMP certificate
- Labeling & Leaflet (Thai leaflet is required)
- Finished product specification
- Documents to support available dosage form/strength, safety and efficacy
- Drug samples

Label (1) Labeling requirement

Labeling information must be in Thai or English

- Name of Product
- Name and amount of active ingredients
- Manufacturer name and address
- Registration number
- Lot no/Batch no
- Mfg.date
- Exp.date
- Quantity - Net wt/vol per packaging

Label (2)

- Thai words in red color "Dangerous drug"or "Specially control drug"or "for topical drug"or "for external use"
- Thai words "for veterinary use"
- Warning as the gazette annoucement
- Withdrawal peroid (food producing animals)
- Storage condition

LEAFLET(PACKAGE INSERT)

Thai leaflet is required

- Product name
- Active ingredients
- Indications
- Instructions for use, including warnings, precautions, adverse drug reactions, and contraindications;
- Dosage
- Storage information
- Withdrawal period for food-producing animals

Part II : Quality Documents (1)

- Application form "Ror yor 1"
- Complete formula/Master formula
- Manufacturing Process
- In-process control
- Raw material specification and test methods
- Finished product specification and test methods

Part II : Quality Document (2)

- Certificate of analysis (COA) of RM, FP
- Packaging specifications & test Method
- Labeling
- Storage condition
- Stability study and report

STABILITY REQUIREMENT(1)

ASEAN Guideline for Stability Studies

STABILITY REQUIREMENT(1)

Temporary Shelf-life

- Minimum 3 batches for one pack size
  - Accelerate data (4 months)+long term data (6 months)
  - or long term data (12 months)
- Tentative Shelf life for 2 years

STABILITY REQUIREMENT(2)

Actual Shelf-life

- Stable active ingredients
  - minimum 2 batches for one pack size
  - long term report
  - Date of initial test & time interval
- Less stable drug substances or biotech product
  - minimum 3 batches one pack size
  - long term report
  - Date of initial test & time interval

New Drugs

Documents required for registration of new drugs

New Drugs

- New Chemical Entities
- New combination
- New delivery system
- New indication
- New strength
- New dosage form
- New species

Documents required for New Drugs Submission (1)

Part I : Administrative Data and Product Information

Part II : Quality Document

- **The same as Generic drugs**

Documents required for New Drugs Submission (2)

Additional Data

Non-Clinical Data

- Pharmacological data Toxicological data
  - Pharmacokinetics
  - Pharmacodynamics

Clinical Data

- Clinical study data in target species

Documents required for New Drugs Submission (3)

Pharmacology
(in target species)

- Pharmacokinetics
- Pharmacodynamics

Pharmacokinetics

- Absorbtion
- Distribution
- Metabolism
- Excretion

Data required for New drug (food producing spp.) submission

- *Toxicology*

(Risk Assessment data)

Ø hazard identification

Ø dose response assess → NOAEL(NOEL) → ADI

Ø exposure assessment → MRL

Ø risk characterization

- Human Safety
- Target Animal Safety
- Environmental Safety
- User Safety
- The analytical method to determine the drug in edible tissue

Data required for New drug (food producing spp.) submission

Toxicology (Risk Assessment Data)

Hazard Identification (or Assessment)

- **General Properties**
- **General Systemic Toxicity Testing**
  - Acute Exposure tests
  - Subchronic Exposure tests (90 days)
  - Long Term Chronic Exposure Test (if available)

Data required for New drug (food producing spp.) submission

Specified Toxicological Testing

- **Reproductive toxicity Testing**
  - Developmental Toxicology and Teratology
- **Genetic Toxicity Testing**
  - Gene Mutation Assay
  - Chromosomal Effect Testing
- **Hepatotoxicity Testing**
- **Nephrotoxicity Testing**
- **Other Toxicity Testing**

Data required for New drug (food producing spp.) submission

Effectiveness (efficacy)

- a study in a target species
- a study in laboratory animal
- any field investigation
- An invitro study (Molecular Mechanism study)

Registration Fee (under Drug Act)

THB 2,000/product

approximate 60 $ US

Ex. Fees under Section 44

Product	Fee		Timeline
	Screening Review (THB)	Scientific Review (THB)	Working Days
New Vet. Drug	2,500	NCE 182,500 Others 155,000	220
Vet. Vaccine	1,000	123,000	160
Generic Vet. Drug	1,000	39,000 (if RM & FPS specifications comply with an official Pharmacopoeia) 49,000	110 120

DRUG VARIATION
(Changes to Registered Drugs)

ASEAN VARIATION GUIDELINE FOR PHARMACEUTICAL PRODUCTS (JULY 2012)

Apply for drug variation approval

- Leaflet
- Packing size
- Label (Distributor)
- Drug appearance
- Product name (add strength/dosage form)
- Formula (excipients only)
- Manufacturing process
- Manufacturing sites
- Analytical method and specification

Withdrawn veterinary drugs (BANNED)

- Hexoestrol
- Chloramphenicol and derivatives and its salts for food producing animal (not including Florfenicol)
- Nitrofurazone
- Furazolidone
- Dimetridazole
- Ronidazole


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