

MALAYSIA REGULATORY SYSTEM FOR PHARMACEUTICAL PRODUCTS

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WHO Collaborating Centre for Regulatory Control of Pharmaceuticals

Member of Pharmaceutical Inspection Cooperation Scheme

MS ISO 9001:2008 Certified

Non-OECD Member full adherence to the Mutual Acceptance Data (MAD) System

Presentation Outline

1. Introduction
2. Legislations
3. Regulatory Components
4. Objective and Expectation
5. Registration Activities
6. Registration Process of Pharmaceutical Products in Malaysia
7. Product Classifications
8. Maintenance of registration

INTRODUCTION

Pharmaceutical Services

- Pharmaceutical Practice and Development Division:
  - Provides comprehensive pharmaceutical care by ensuring efficient selection, procurement, distribution of pharmaceuticals; ensuring rational; cost-effective and optimal use of medicines through effective up-to-date clinical and professional pharmaceutical services in tandem with the current global development.

- Pharmacy Management Division:
  - Consolidates the pharmaceutical sector activities through the implementation of the National Medicines Policy

- The Pharmacy Enforcement Division was formed on January 1, 1976 under the PSD to carry out the enforcement of legislations pertaining to pharmacy and the pharmaceutical trade in the country in a more efficient approach.

- National Pharmaceutical Control Bureau (NPCB):
  - As National Drug Regulatory Authorities in Malaysia
  - Was given the task of ensuring the quality, efficacy and safety of pharmaceuticals through the registration and licensing scheme.

PSD: Program Strategies

- Ensuring the safety, efficacy and quality of pharmaceuticals including traditional medicines via product registration, licensing of premises, monitoring of adverse drug reactions and market surveillance
- Improving enforcement of existing Acts and Regulations by strengthening enforcement units, formulating new legislations and intensifying enforcement at entry points
- Ensuring a continuous and adequate supply of quality pharmaceuticals by expanding and improving storage facilities, modernizing the inventory management system and utilizing ICT
- Strengthening hospital pharmacy services by improving infrastructure, promoting rational use of drugs and enhancing clinical pharmacy activities through provision of various services
- Maintaining adequate manpower and increasing competency of personnel through various human resource development programs

LEGISLATIONS

- **MALAYSIAN LAWS ON POISONS AND SALE OF DRUGS**

- <u>CONTAINS:</u>
- Dangerous Drug Act 1952 (revised 1980)
- Poisons Act 1952 (Act 366) & regulations
- Sale of Drugs Act 1952 (Act 368)
  - **Control of Drugs and Cosmetics Regulations 1984**
- Registration of Pharmacists Act 1951 (Act 371) & regulations
- Medicines (Advertisement and Sale) Act 1956 (Act 290) & regulations

LEGISLATIONS

Control of Drugs and Cosmetics Regulations (CDCR) 1984

Regulation 7(1)

No person shall manufacture, sell, supply, import, possess or administer any product

unless:

(a) the product is a registered product,

and

(b) the person holds the appropriate license required & issued under these Regulations.

LEGISLATIONS

Regulation 12 of CDCR 1984: Licenses

- *a **manufacturer's licence**, authorising the licensee to manufacture the registered products in the premises specified in the licence and to sell by wholesale or supply the products;*

- *a **wholesaler's licence**, authorising the licensee to sell by wholesale or supply the registered products from the address of the business premises specified in the licence;*

- *an **import licence**, authorising the licensee to import and sell by wholesale or supply the registered products from the address of the premises specified in the licence. – therefore, imported product can be imported into Malaysia by an importer who holds the import license for a particular registered product.*

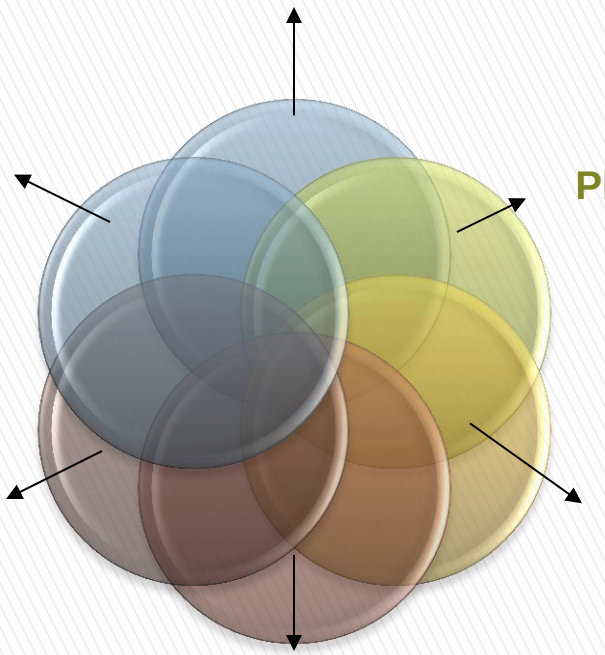
LEGISLATIONS

- **The Drug Control Authority (DCA) : as the licensing authority (Regulation 3, CDCR 1984).**

- **National Pharmaceutical Control Bureau (NPCB) acts as its secretariat & is responsible for:**
  - **Product registration and cosmetic notification**
  - **Licensing (manufacture, import, wholesale)**
  - **Monitoring and surveillance activities.**

Overview of Regulatory Control :

Regulatory Components



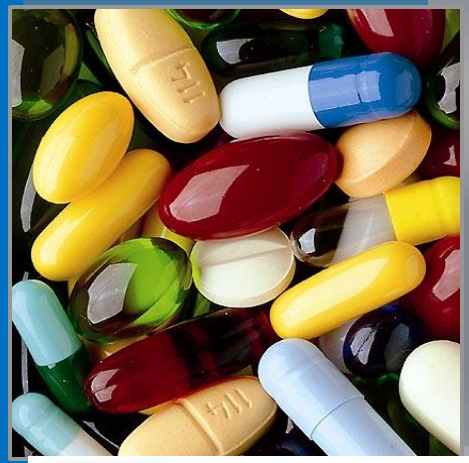
OBJECTIVE

To ensure that therapeutic substances approved for the local market are SAFE, EFFICACIOUS and of QUALITY and also to ensure that cosmetic products approved are safe and of quality.

EXPECTATIONS

Patients	• Expect treatment using new medical innovations • Timely access to new drugs
Prescribers	• Expect drugs to be reviewed in approved in a judicious manner • Expect drugs to be of quality, efficacious, safe
Industry	• Reduction in bureaucratic procedures • Harmonisation of standards and technical requirements

REGISTRATION ACTIVITIES

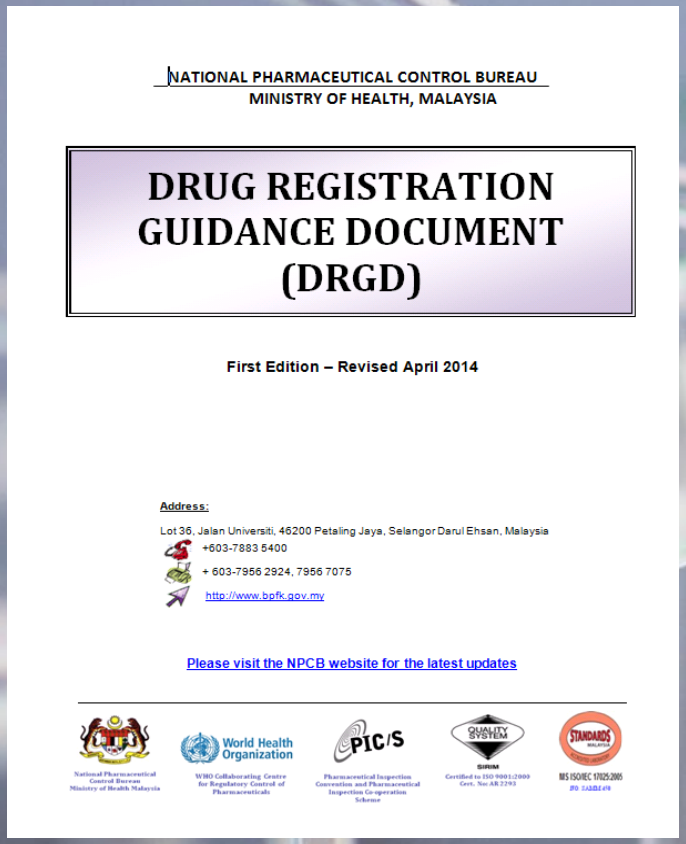


Registration

- **Product classification**
- **Registration process**
- **Tools – Guidelines, Check-lists, SOPs**
- **Evaluation of Quality, Safety and Efficacy**
- **Marketing Authorization**
- **Additional Indication of New Chemical Entities (NCEs) & Biotech Products**
- **Variations – notification, approval**
- Certificate of Pharmaceutical Product (CPP) , Certificate of Free Sale (CFS)
- **Renewals**
- **Appeals**
- **Current Status**

- **Product Classification Guidelines**
- **Product Registration Guidelines**
- **Guidelines for Site Change**
- **Guidelines for Variations**
- **Guidelines for Blood Products**
- **Guidelines for Vaccines**
- **Stability Studies Guidelines**
- **Bioavailability/Bioequivalence Studies**
- **Audit of BA/BE Centers (draft)**
- **Good Clinical Practice**
- **Clinical Trial Import Licence**
- **ASEAN Common Technical Dossier**
- **ASEAN Process Validation**
- **ASEAN Analytical Validation**

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD)



NATIONAL PHARMACEUTICAL CONTROL BUREAU
MINISTRY OF HEALTH, MALAYSIA

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD)

First Edition – Revised April 2014

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http://www.bpfk.gov.my

Please visit the NPCB website for the latest updates

DRGD serves as a reference guide for both pharmaceutical products for human use and natural products.
(Latest revision: January 2015)

A separate guideline is available for registration of Veterinary products and Cosmetics

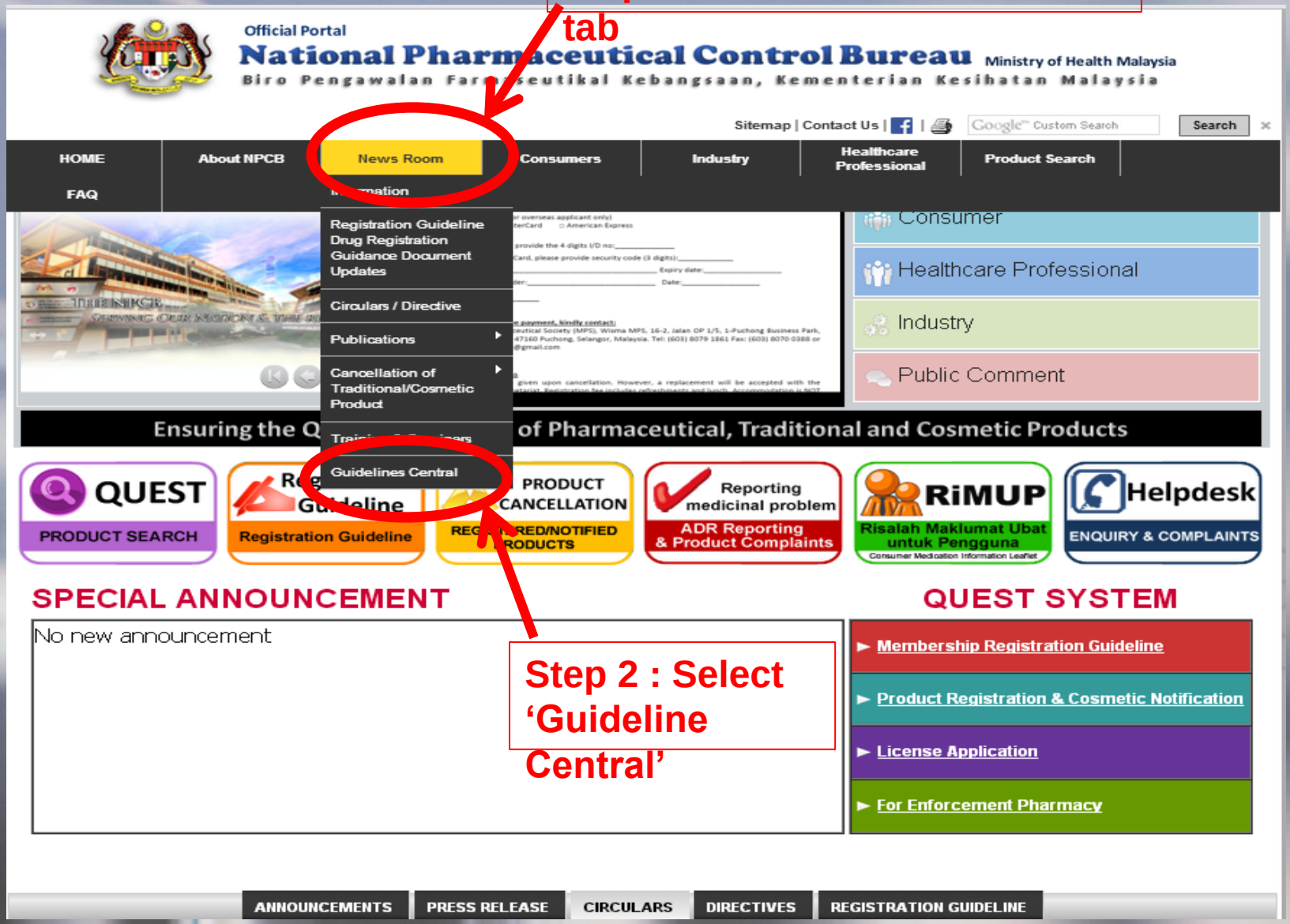
Outline of DRGD

- **Section A:** General Overview
- **Section B:** Product Registration Process
- **Section C:** Quality Control
- **Section D:** Inspection & Licensing
- **Section E:** Post-Registration Process
- **Appendices**

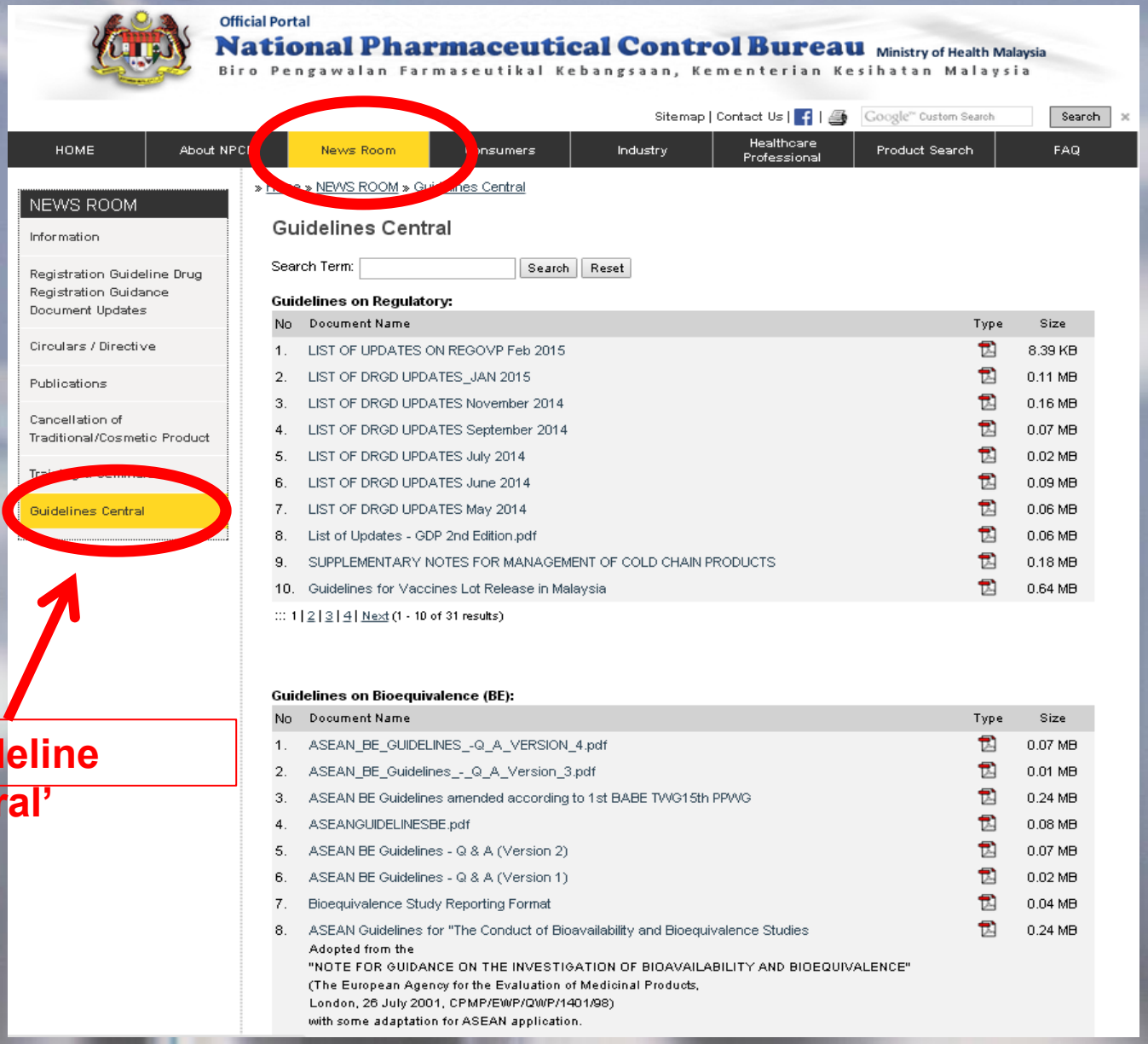
Appendices

No.	Appendices	Title of Appendix
1.	Appendix 1	Fees
2.	Appendix 2	Requirements For Product Registration
3.	Appendix 3	Guidelines On Registration Of Biologics
4.	Appendix 4	Guideline On Registration Of Health Supplements
5.	Appendix 5	Guideline On Registration Of Natural Products
6.	Appendix 6	Guideline On Regulatory Control Of Active Pharmaceutical Ingredients (API)
7.	Appendix 7	Special Conditions For Registration For A Particular Product Or Group Of Products
8.	Appendix 8	List Of Permitted, Prohibited And Restricted Substances
9.	Appendix 9	Labelling Requirements
10.	Appendix 10	Guideline On Patient Dispensing Pack For Pharmaceutical Products In Malaysia
11.	Appendix 11	Guideline On Filling The Online Application Form For Product Registration Via Quest System
12.	Appendix 12	Conditions And Supporting Documents Required For An Application Of Variation
13.	Appendix 13	Supporting Documents Required For Change Of Manufacturing Site (Cos) Application
14.	Appendix 14	Guidelines On Safety Data Requirements For Complementary Medicine Products

Steps for searching 'Guidelines' at BPFK website

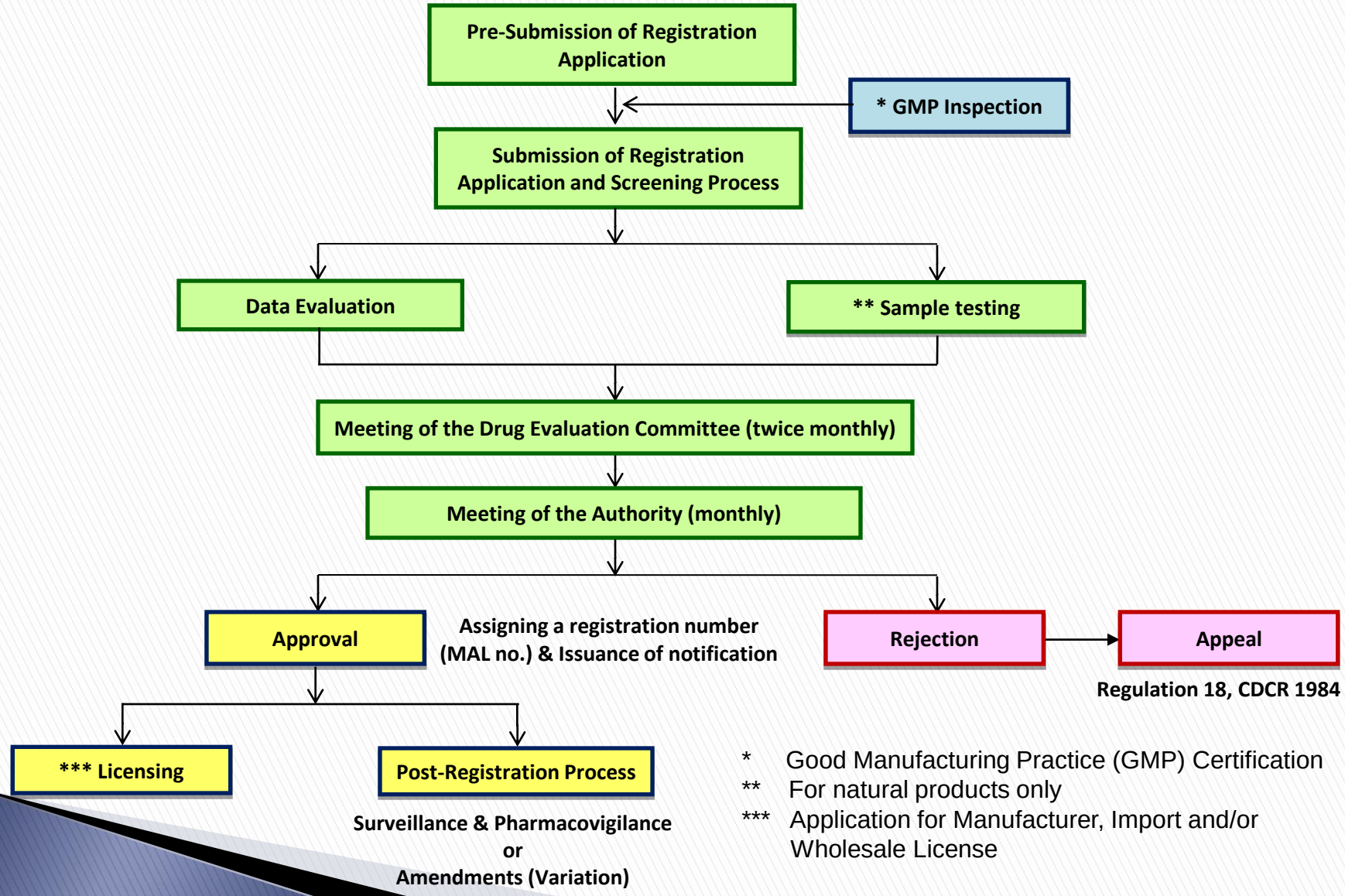


Listing of Guidelines at BPFK website



'Guideline Central'

Overview of Product Registration Process



* Good Manufacturing Practice (GMP) Certification
** For natural products only
*** Application for Manufacturer, Import and/or Wholesale License

Official Portal

National Pharmaceutical Control Bureau

Ministry of Health Malaysia

Biro Pengawalan Farmaseutikal Kebangsaan, Kementerian Kesihatan Malaysia

Sitemap | Contact Us | | Google™ Custom Search Search

HOME | About NPCB | News Room | Consumers | Industry | Healthcare Professional | Product Search | FAQ

- General Information
- Drug Registration Guidance Document (DRGD)
- Regulatory Information
- Registration and Notification
- Inspection
- Licensing
- New Products/Indication
  - New Products Approved (QUEST3)
  - New Products Approved (QUEST2)
  - New Chemical Entities
  - Additional Indications Approved
- Laboratory & Quality Control
- Forms
- Clinical Trial
- Good Laboratory Practice (GLP) Compliance Monitoring Programme
- Quest2 List of Manufacturers / Wholesales / Importers

Consumer

Healthcare Professional

Industry

Public Comment

Ensuring the Quality and Safety of Pharma... ...nal and Cosmetic Products

QUEST
PRODUCT SEARCH

Registration Guideline
Registration Guideline

PRODUCT CANCELLATION
REGISTERED/NOTIFIED PRODUCTS

Helpdesk
ENQUIRY & COMPLAINTS

SPECIAL ANNOUNCEMENT

No new announcement

QUEST SYSTEM

▶ Membership Registration Guideline

CATEGORIES OF PRODUCTS

Product....

Regulation 2: Interpretation, under the Control of Drugs and Cosmetics Regulations 1984,

'Product' means :

- **a 'drug' in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for a medicinal purpose; or**
- **a drug to be used as an ingredients of a preparation for a medicinal purpose.**

- The products include, but not limited to the following:
- Pharmaceutical products containing scheduled poisons
- Pharmaceutical products containing non-scheduled poisons
- (For examples: Medicated plaster with medicine, antiseptic/ disinfectants for use on the human body, diagnostic agents for human use (in-vivo) and health supplement such as probiotics and chitosan)
- Natural products - Includes herbal and traditional products

INNOVATOR PRODUCT

1) New Drug Products (NDP)

- defined as any pharmaceutical product that has not been previously registered in accordance with the provisions of the CDCR 1984.

1) New Drug Products (NDP)

- An NDP may be classified according to the following categories:

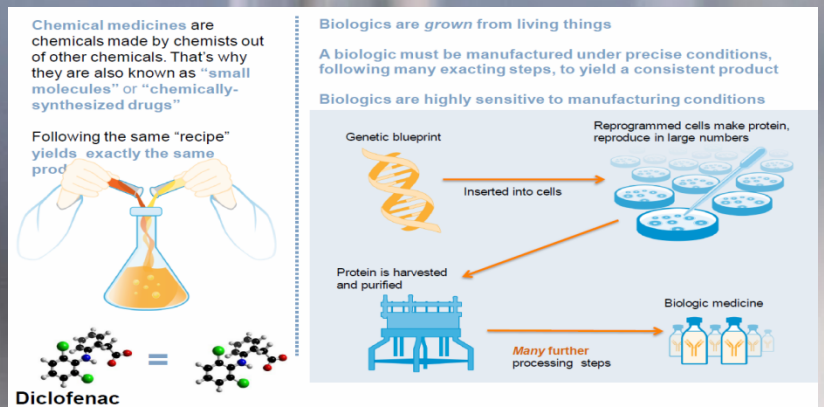
a) **New Chemical Entity (NCE):** An active moiety that has not been registered in any pharmaceutical product.

b) **New combination product:** A new pharmaceutical product containing two or more drugs that are physically, chemically or otherwise combined or mixed and produced as a single pharmaceutical product, in a combination that has not been registered in any other pharmaceutical product.

c) **Supplemental product:** A new pharmaceutical product containing a drug that has been previously registered as a pharmaceutical product but differing in properties with regards to safety and/or efficacy from the product that has been previously registered.

2) Biologics

- Refers to a product whose active substance is made by or derived from a living organism (plant, human, animal or microorganism) and may be produced by biotechnology methods and other cutting-edge technologies. This product imitates natural biological substances in our bodies such as hormones, enzymes or antibodies.



Biologics include a wide range of products such as:

- Vaccines;
- Blood products;
- Monoclonal antibodies (therapeutics);
- Recombinant proteins:
- Insulins
- Hormones
- Erythropoetins and other hematopoietic factors
- Cytokines: Interferons, interleukins, colony-stimulating factors, tumour necrosis factors.

Moving forward

- Emerging categories of therapeutic products:
  - –Cellular and gene therapies
  - –Antibody-drug conjugates
  - –Therapeutic vaccines

GENERIC PRODUCT

- A product that is essentially similar to a currently registered product in Malaysia. The term generic is not applicable to biologic products.

3) Scheduled Poison:

- Known as Controlled Medicine/ Controlled Poison
- Pharmaceutical products which contain scheduled poison(s) as listed in the First Schedule under the Poisons Act 1952.

4) Non-Scheduled Poison:

- Known as Non-Poison or “Over-the-Counter”, OTC
- Products containing active ingredients which are not listed in the First Schedule under Poisons Act 1952; and is excluding active ingredient which is categorized under health supplements or natural products or cosmetics.

5) Health Supplements

- Any product that is used to supplement a diet and to maintain, enhance and improve the health function of human body. It is presented in small unit dosage forms (to be administered) such as capsules, tablets, powder, liquids and shall not include any sterile preparations (i.e. injectables, eyedrops). It may contain one or more, or the following combination:

❖ Vitamins, minerals, amino acids, fatty acids, enzymes, probiotics, and other bioactive substances;

❖ Substances derived from natural sources, including animal, mineral and botanical materials in the forms of extracts, isolates, concentrates, metabolite;

❖ Synthetic sources of ingredients mentioned in (i) and (ii) may only be used where the safety of these has been proven.

6) TRADITIONAL MEDICINE

- Any product used in the practice of indigenous medicine, in which the drug consists solely of one or more naturally occurring substances of a plant, animal or mineral, or parts thereof, in the unextracted or crude extract form and a homeopathic medicine (as defined under the CDCR 1984).
- It shall not include any sterile preparation, vaccines, any substance derived human parts, any isolated and characterized chemical substances.

7) Veterinary Products

- Refers to pharmaceutical products for animal use.
- To protect the health of the consumer from food-producing animal as well as to ensure that foods obtained from animals treated with veterinary products **must not contain residues of the drug (Minimum residual limit, MRL)** or its **metabolites** which might constitute a health hazard for the consumer.
- To ensure only **quality** and **safe** products are registered and marketed in Malaysia.

IMPLEMENTATION DATE

- Implementation date : 1 August 2007
- The implementation of the regulations on veterinary products shall be on all **products** containing scheduled poisons and non – scheduled poisons intended to be administered to the animals for **medicinal purpose**
- Dietary/health supplements and herbal/natural preparations are controlled by DVS under Feed Act 2009 starting 1st July 2014.
- Medicated Feed is controlled by DVS under Feed Act 2009 starting 1st January 2015.
- Premixes (antibiotics for prevention and growth promotion) will be controlled by DVS under Feed Act 2009 starting 1st July 2015.

REGULATION OF VETERINARY PRODUCTS

Products containing:
1) Scheduled Poison (as in First Schedule of Poison Act 1952)
2) Non Scheduled Poison / OTC
3) Pesticides for Internal Use
4)Pesticides for External Use (Control of endoparasite)

BPFK

Products containing:
1) Animal feed
2) Feed additives
3) Health/Dietary Suplement
4) Herbal/Natural

Department of Veterinary Services (DVS)

Products containing:
1) Pesticides as listed under First Schedule of Pesticide Act 1974 for External Use only.(e.g. Azadirachtin which contains in *Azadirachta indica* (**Neem**)

Pesticide Board

PRODUCT REGISTRATION

CRITERIA FOR :

COSMETICS :	**Safety & Quality**
	Product Information
TRADITIONAL :	**Safety & Quality** **Product Information** **“Traditionally used”**
Pharmaceuticals:	**Safety, Quality & Efficacy**
	Product Information

Registration Criteria (Quality, Safety, Efficacy)

Product Name
Product Description
Pack size
Type of container

Products Particulars

Product Formulation

Banned ingredient
Limits
Product testing
FPQC, Stability

Manufacturer
- **GMP**
- **CPP**
- **CFS**

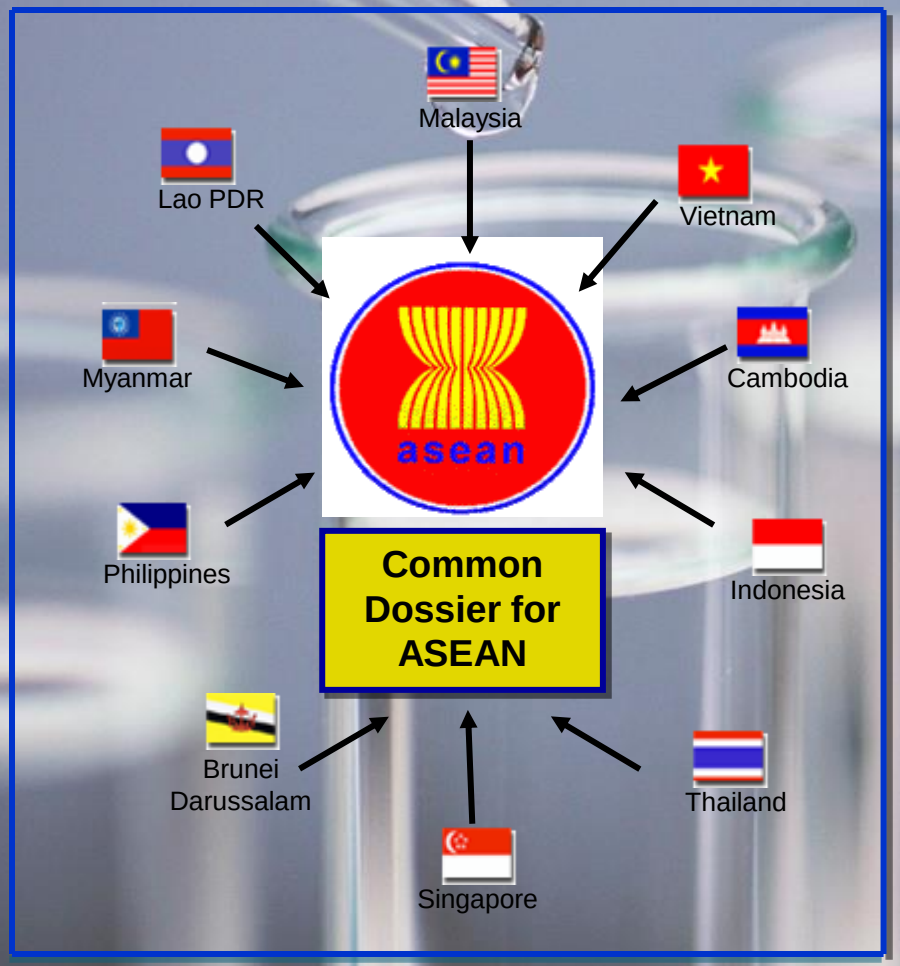
Compulsory labeling requirement
Additional Warning/ Precaution

Bioequivalence/ Bioavailability Studies

Labeling Requirement

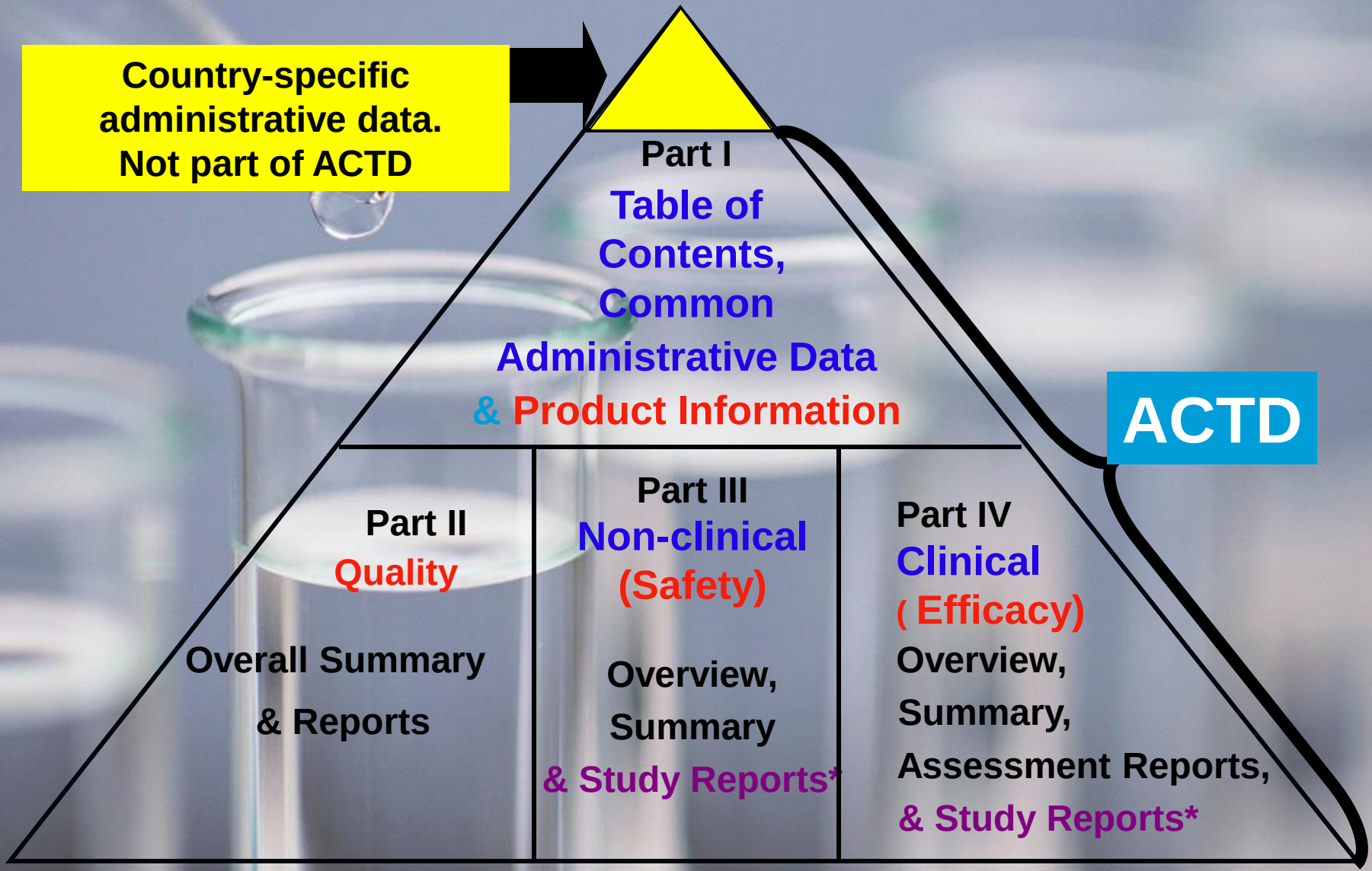
Interchangeability

With the advent of globalisation, efforts are currently undertaken towards ASEAN Harmonisation process.



- Pharmaceutical Product Working Group – ASEAN Consultative Committee for Standards and Quality (PPWG-ACCSQ)
- Objective is to develop harmonization schemes of pharmaceutical regulations of the ASEAN member countries to complement and facilitate the objective of AFTA, particularly the elimination of technical barriers to trade posed by regulations, however without compromising product quality, efficacy and safety.
- **ASEAN Common Technical Dossier/Requirements**
- ASEAN Technical Documents – Process Validation, Analytical Validation, Stability, BA/BE

Organization of Application Dossier



* Upon Request

Requirement for Registration

ASEAN Common Technical Document (ACTD)

Part I – Administrative Data & Product Information

Part II – Quality

Part III – Non-Clinical Data

Part IV – Clinical Data

PRODUCT REGISTRATION

Quality

- Certificate of Pharmaceutical Product : GMP Certificate & Certificate of Free Sale
  - GMP inspection : Basic GMP Requirement
    - Premise, Location and facilities,Equipment and quality control
    - Testing procedures and Standard Operating Procedures
    - Products security,Manufacturing records and recall procedures
    - Self Inspection

- Product Testing :
    - Product Specifications: Compendial/Non-compendial
    - Heavy metals : Pb, Hg, As
    - Microbial Limit Test

PRODUCT REGISTRATION

Safety

- Preclinical Data : Animal studies/ Toxicology Studies
- Clinical safety Data : SAE & ADR reporting from Clinical Studies, Periodic Safety Update Report , ADR monitoring
- Non Permitted Ingredients : Eg. phenylpropanolamine(ppa), penicillin for topical use, tartrazine, cyclamate, Magnolia Officinalis,
- Screening of heavy metals in Traditional Products
- Product Information : warning labels/precautions/drug interactions/adverse effects

PRODUCT REGISTRATION

EFFICACY : PHARMACEUTICALS

- Clinical Efficacy Data : Clinical Trials, Phase 2 and 3
  - **New Chemical Entity :** New chemical not previously authorized for marketing for any pharmaceutical use in the country .
  - **Biologicals/Biotechnology Products :** Any product of biological origin, prepared with biological processes, derived from human blood and plasma, or manufactured by biotechnology, consisting of substances of higher molecular weight whose purity, potency, and composition cannot readily and reliably be determined by chemical or physicochemical analysis . *(Examples of this group include vaccines, blood products, modified animal tissues, high-molecular-weight hormones, allergens, and the products of genetic engineering or other newer biotechnological techniques*
- **Bioequivalence Studies**
  - **Generics/Multisource/Copy /Me-too Products :** A pharmaceutical product usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after expiry of the patent or other exclusivity rights

Application Procedure

- Registration of products shall be done via a web-based QUEST online system at http://www.bpfk.gov.my
- Applicant must first register a membership for QUEST system with NPCB and purchase a USB Token that contains a User Digital Certificate from Digicert Sdn. Bhd.
- Submission of data can be done at anytime - 24 hrs a day, 365 days a year, from any part of the world

Fees
(effective January 2007)

No	Product Categories	Processing Fees (RM)	Analysis Fees (RM)	Total Fees (RM)
1	**Pharmaceutical (New Drug Products & Biologics)**	1,000.00	Single active ingredient : 3,000.00	4,000.00
			Two or more active ingredients : 4,000.00	5,000.00
2	**Pharmaceutical (Generics and Health Supplements)**	1,000.00	Single active ingredient : 1,200.00	2,200.00
			Two or more active ingredients: 2,000.00	3,000.00
3	**Natural Products**	500.00	700.00	1,200.00

The processing fee is NOT REFUNDABLE [CDCR Reg. 8(4)]

FEES FOR VETERINARY PRODUCTS

Processing fee + analysis fee:

- For Scheduled Poison, Non-Scheduled Poison : **RM1,500**
- For Export Only-Scheduled Poison : **RM 500**
- For Export Only-Notification for Other than Scheduled Poison : **RM 100**

Timeline

No.	Product Category	* Duration (Inclusive screening process)
(A)	**Full Evaluation**	
1.	New Drug Products	245 working days
2.	Biologics	245 working days
3.	Generics (Scheduled Poison)	210 working days
4.	Generics (Non-Scheduled Poison)	210 working days

* Upon receipt of complete application.

Timeline

No.	Product Category	*Duration (Inclusive screening process)
(B)	**Abridged Evaluation**	
5.	Generics (Non-Scheduled Poison) (Product categories as stated in Table V above)	80 working days
6.	Natural Products a) Single active ingredient b) Two (2) or more active ingredients	a) 116 working days b) 136 working days
7.	Health Supplements a) ** Single active ingredient b) ** Two (2) or more active ingredients ** *Applicable for:* *i) General or Nutritional Claims; and* *ii) Functional Claims (Medium Claims)* c) Disease Risk Reduction Claims (High Claims)	a) 116 working days b) 136 working days c) 245 working days

***** Upon receipt of complete application.

MAINTENANCE OF REGISTRATION

Maintenance of registration

- Registration number: MAL YYMM$$$$##

E.g. MAL11070001AR

Code(##):

A= Scheduled Poisons
X= Non-scheduled Poisons
N= Health Supplement
T= Natural Products/ Traditional Medicines
H= Veterinary Product
C= Contract Manufactured
E= For Export Only (FEO)
R= Repacked
S = Second source
Y= Orphan product
Z= Products listed under the National Essential Medicine List (NEML) for zero rated Government Services Tax (GST)

Cosmetic product : NOT *******K eg: NOT1234567K

Maintenance of registration

- **Validity period of registration – 5 years**
- **Renewal of product registration shall be done not later than 6 months prior to expiry of product registration, e.g. 7 Sept 2011 (expiry) – 7 Mac 2011 onward shall submit renewal application.**
- **Updating of product information/ amendments/ variations is allowed through proper application (via post-registration centre)**
- **Any changes that would affect the quality, safety and efficacy of a registered product is not be allowed. E.g. to change formulation. New registration shall be submitted.**

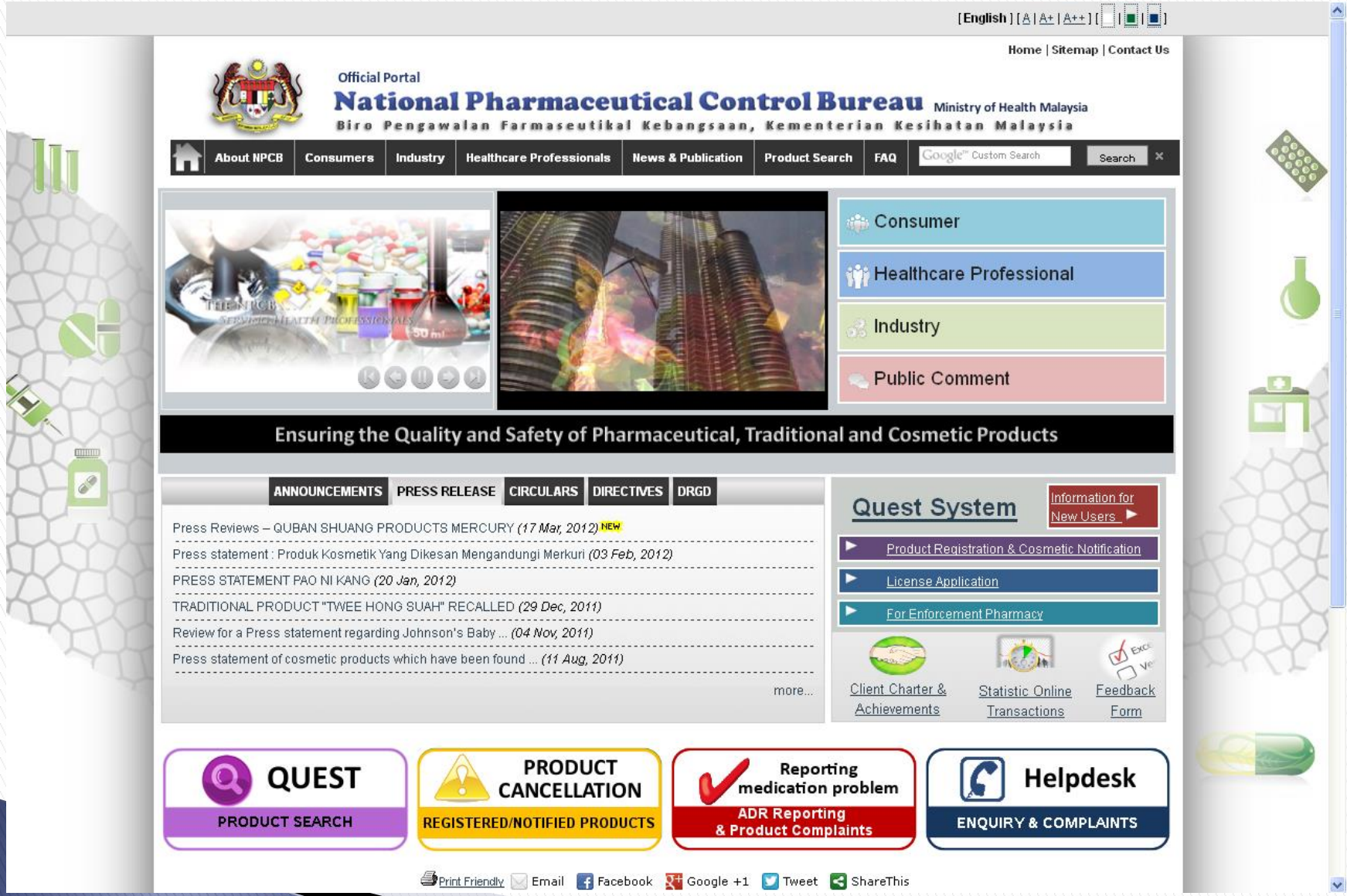
Maintenance of registration

- Post-Market Surveillance (PMS), Adverse Drug Reaction Monitoring and investigation on complaints will be done from time to time.
- The DCA wishes that all medical practitioners, health professionals, consumers and the public report any complaints regarding the quality of medicines particularly if they experience adverse reactions or any other problems with these medicines.
- The DCA will not hesitate to suspend, cancel, recall unsafe or substandard products from the market.

The Way Forward

Hosting of 1st Malaysia-Japan Symposium	March 2015
Hosting of ACCSQ-TMHS	June 2015
Organising the National Regulatory Conference	Aug 2015
3rd Technical Meeting of the OIC - Development & Harmonization of Standards on Pharmaceutical & Vaccines	Nov 2015
Control of Cellular & Gene Therapy Products (CGTP)	2015
Registration of high/medium claims for herbal products	2015

NPCB Website: www.bpfk.gov.my



THANK YOU!

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