WHO Collaborating Centre for Regulatory Control of Pharmaceuticals

Member of Pharmaceutical Inspection Co-operation Scheme

SIRIM
Certified to ISO 9001:2008
Cert. No.: AR 2293

MS ISO/IEC 17025:2005
Certified to MS ISO/IEC:17025:2005
NO: SAMM 450

DRUG REGULATORY SYSTEM IN MALAYSIA
OVERVIEW and UPDATES

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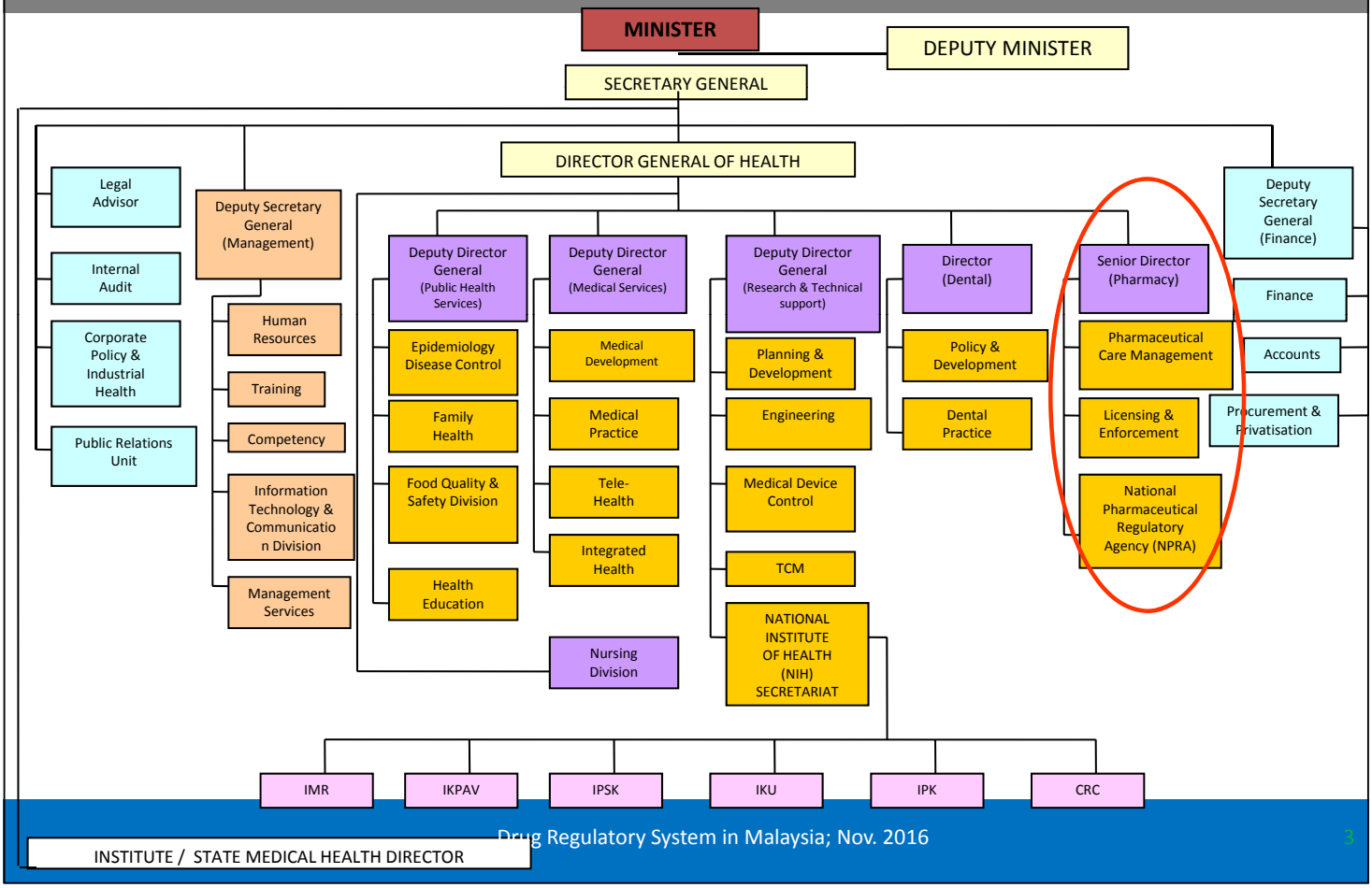
Ministry of Health Malaysia

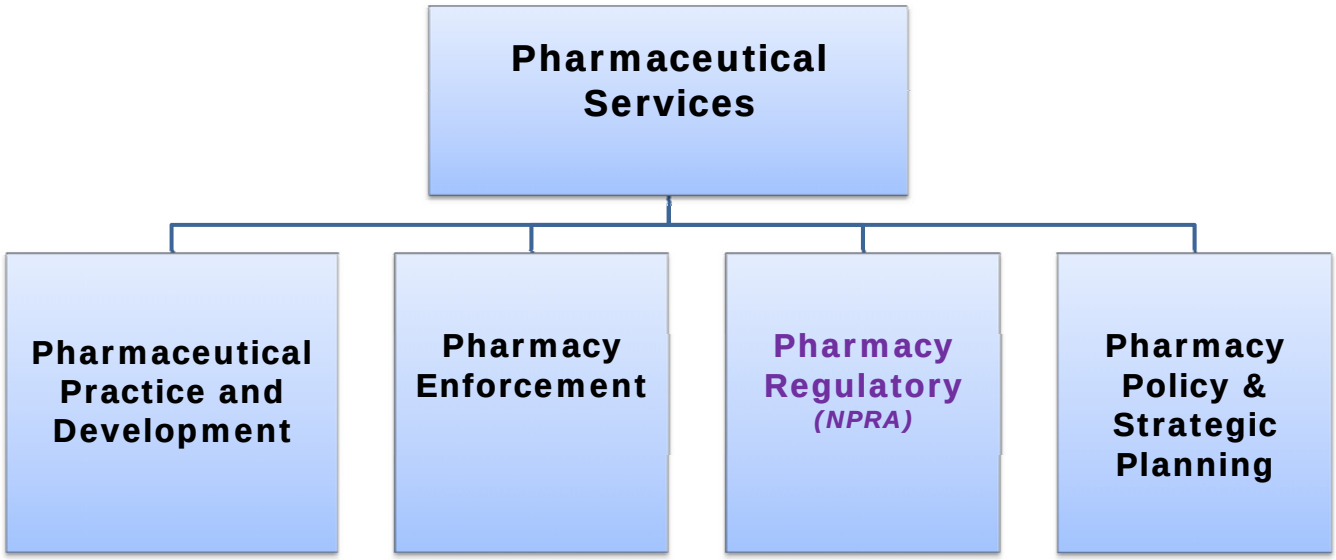
Presentation Outline

- Introduction of NPRA
- Drug Regulator System/ Activities
- Product Registration
- Regulatory Updates
- Statistics

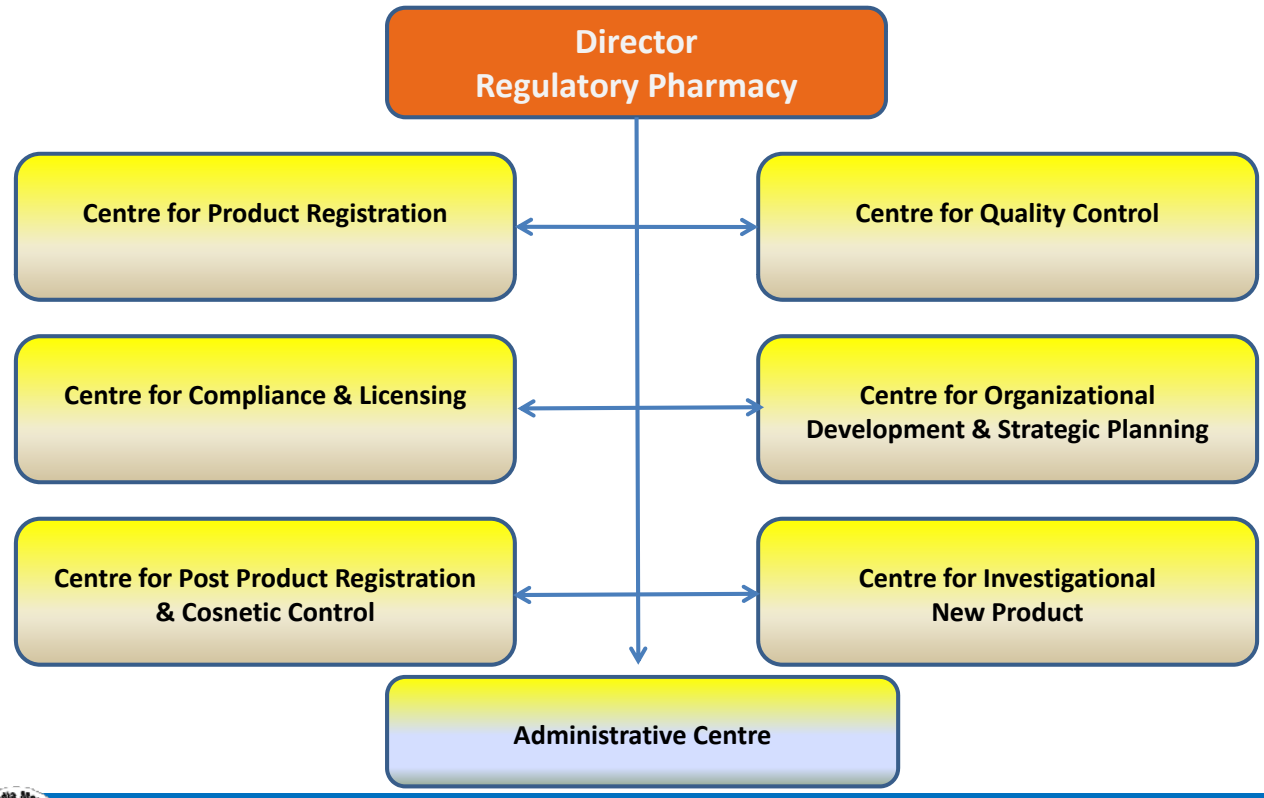
Ministry of Health Malaysia



Pharmaceutical Services



Organisation of NPRA



Vision and Mission

Vision of NPRA

- To be a world renowned regulatory authority for medicinal products and cosmetics

Mission of NPRA

- To safeguard the nation's health through scientific excellence in the regulatory control of medicinal products and cosmetics

Laws and Regulations

- Sales of Drugs Act 1952 (rev. 1989)

  Control of Drugs and Cosmetics Regulations 1984 (ammend 2009)
- Dangerous Drug Act 1952 (rev. 1980)
- Poisons Act 1952 (rev. 1989)
- Medicines (Advertisement and Sale) Act 1956 (rev. 1983)
- Registration of Pharmacist Act 1951 (rev. 1989)
- Others - Patent Act 1983,

  Trade Description Act 1972,

  Pesticides Act 1974,

  Food Act 1983 and Food Regulations 1985

Meet the Expectation

Patients

- Expect treatment using new medical innovations
- Timely access to new drugs
- Accountability
- Trust

Prescribers

- Expect drugs to be reviewed and approved in a judicious manner
- Expect drugs to be of quality, efficacious, safe
- Timely access
- Flexibility
- Responsiveness
- Confidence

Industries

- Reduction in bureaucratic procedures
- Harmonization of standards and technical requirements
- Predictability

Drug regulatory system

An effective and efficient drug regulatory system in place;

- To ensure quality, safety and efficacy of pharmaceuticals through the marketing approval and licensing scheme

- Productivity and efficiency of marketing approval process is expected to increase
  - Provided that all applications are COMPLETE, IN PROPER ORDER and ACCURATE

Drug regulatory system

Key functions of regulation of drugs encompasses;

- product assessment & registration,
- licensing of premises,
- on site inspection of manufacturing facilities & distribution channels,
- adverse drug reaction monitoring,
- post market surveillance,
- quality control analysis,
- control of drug promotion & advertising,
- control of clinical trials,
- enforcement,
- consumer education

Regulatory Components

Registration

- Evaluate & register products
- issue CPP (Certificate of Pharmaceutical Product), CFS (Certificate of Free Sales)

Education

- Provide training – in-house training as well as training for visitors from overseas.
- Disseminate product information

Pharmacovigilance

- Adverse drug reaction (ADR) monitoring
  - to ensure each product marketed is safe & effective to the public

Inspection & Licensing

- Inspection of premises
- Issueance licenses (Manufacturers, Importers, & Wholesalers)
- Issueance Clinical Trial Import License

Surveillance

- Post-registration market surveillance
  - audit activity to companies to collect samples for checking samples / lab testing

Analysis

- Analysis of samples
  - pre- and post-registration products
  - testing of complaint cases
  - adulterated samples from CPF (Enforcement) after raiding activity

Functions of NPRA

- Evaluation and Registration of Products
- Sample analysis
- On site Inspection
- Issuance of Licenses & Certificates
- Post-registration market surveillance
- Adverse Drug Reaction (ADR) monitoring
- Dissemination of drug information
- Training
- International & Regional collaboration

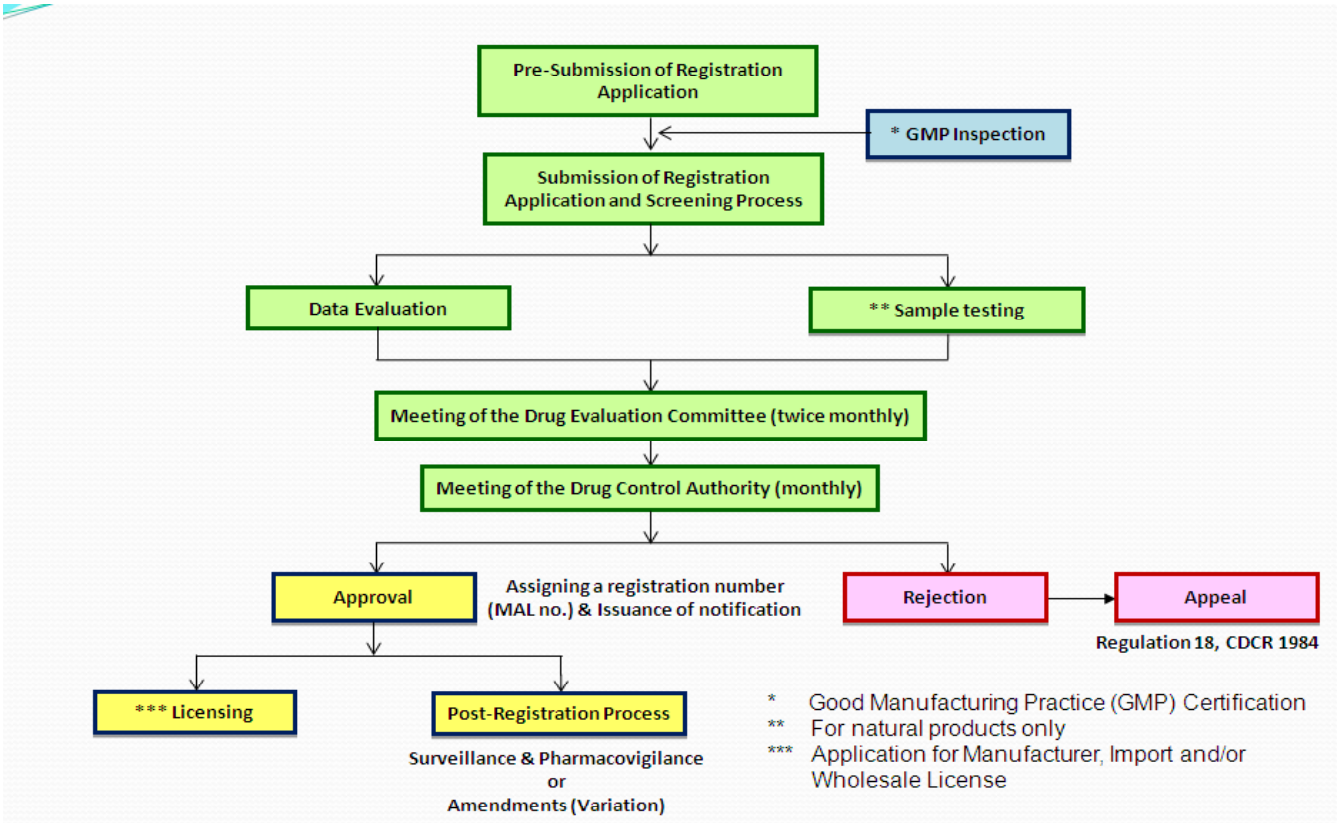
Registration Phases

Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6	Pha
Registration of Prescription Drugs (Aug. 1985)	Registration of Non Prescription (OTC) (Jan.1988)	Registration of Herbal/Trad. Medicine (Jan. 1992)	Registration of Cosmetics (Feb. 2002)	Registration of Veterinary Med. (Aug. 2007)	Regulatory control of API (2012)**	
Licensing May 1987	Licensing 1992	Licensing Manufacturers & Importers Jan 1999 Wholesalers July 2002	Licensing Jan 2004	Licensing 1 Jan 2012	No licensing Requirements as registration of API is linked to products	
Surveillance 1990	Surveillance 1995	Surveillance 2000	Surveillance 2005	Surveillance 2016	Surveillance (to be announced)	

- **Regulatory control of API**
  - NCE - January 2012
  - Generic products containing Scheduled Poison
    - Parenteral – July 2014
    - Oral dosage form – July 2016
    - Others – July 2018

Registration Criterias

Product Registration Process



On line Registration (QUEST system)

Paperless submission using web-based application accessible via internet connectivity

Submission of data can be done at anytime - 24 hrs a day, 365 days a year, from any part of the world

Process includes:

- Application submission
- Filing, editing, completing and submitting registration forms
- Receiving & replying to memos (inclusive of e-mail notification)
- Change Requisition Processes
- Approval, Certification and
- Product Registration Renewal

QUEST system

- On-line web-based system since:
  - 2000 – QUEST 1
  - 2002 – QUEST 2
  - 2010 – QUEST 3

- QUEST 3+ - to be launch in January 2017

Agency Update

From 1 August 2016..

National Pharmaceutical Control Bureau (NPCB)

is known as

National Pharmaceutical Regulatory Agency (NPRA)

NPRA MALAYSIA NATIONAL PHARMACEUTICAL REGULATORY AGENCY

Regulatory Updates - 1

- Use of generic name as product name
  - Pharmaceutical products are **NOT** allowed to use generic name (International Proprietary Name, INN) as stand- alone for product name.
  - Use of generic name as product name should be simultaneously with a name other than generic name to enable differentiation between products and to avoid confusion among public.
  - For example, product name Atenolol Table 50mg is not allowed, whereas <XYZ> Atenolol Tablet 50mg is allowed.
- Effective date
  - New Registration: **21 Dec 2015**
  - Existing Products: **1 Jan 2017**

Regulatory Updates - 2

- Certain Products previously regulated as pharmaceuticals is currently regulated as medical devices
  - Hemodialysis solutions, medicated plaster etc
  - Enforcement: Extended to July 2016
  - Allowed to be renewed as pharmaceuticals until this date
  - Future Plans: To be accreditated under ISO 13485

Regulatory Updates - 3

- Regulatory control of API in registered pharmaceutical products containing scheduled poisons (all dosage forms)
  - Products with registrations that expire 1st January 2020 onwards
  - The registration holder must submit documents with the required API information **at least 1 year** before the registration expires
  - Implementation date of control of API for new applications:
    - Parenteral dosage form → **1 July 2014**
    - Oral dosage form → **1 July 2016**
    - Other dosage forms → **1 July 2018**

Regulatory Updates – 4.1

- Amendment on Package Insert (with request for variation to be submitted to NPRA) for Products containing;
  - Azithromycin
    - To include safety information regarding Adverse Event of Prolongation of the QT interval and Drug reaction with Eosinophilia and Systemic Symptoms (DRESS)
      - ✓New Application/ Product under evaluation: **1 March 2016**
      - ✓Existing : **1 September 2016**

Regulatory Updates – 4.2

- Amendment on Package Insert (with request for variation to be submitted to NPRA) for Products containing;
  - Mycophenolate (Mycophenolate Mofetil/ Mycophenolic Acid)
    - To include safety information regarding risk of teratogenic effect
      - ✓New Application/ Product under evaluation: **1 June 2016**
      - ✓Existing : **1 December 2016**

Regulatory Updates – 4.3

- Update Package Insert for Products containing;
  - Biphosphonate (Alendronate, Clodronate, Ibandronic Acid, Pamidronate, Risedronate, Zoledronic Acid)
    - To include safety information regarding Adverse Event of Osteonecrosis of the External Auditory Canal
      - ✓New Application/ Product under evaluation: **1 July 2016**
      - ✓Existing : **1 January 2017**

Regulatory Updates – 4.4

- Update Package Insert for Products containing;
  - Cajeput Oil (Melaleuca Leucadendra) in topical dosage form
    - To include safety information regarding risk of breathing problem/ shortness of breath
      - ✓New Application/ Product under evaluation: **1 August 2016**
      - ✓Existing : **1 January 2017**

Regulatory Updates – 5.1

- Bioequivalence (BE) Report Required for;
  - All scheduled Poisons formulated in Tablet/ Capsules formulated as effervescent, dispersible, orodispersible, sublingual, buccal, chewable
  - Effective date - extended
    - New Application: **1 January 2018**
    - Existing : **1 January 2019**
  - Circular: 31 May 2016

Regulatory Updates – 5.2

- Directive on Assesment of Bioequivalence (BE) Study Centre Inspection Reports for Registration of Products
  - Assesment of BE Study Centre Inspection Reports by recognized DRAs (such as USFDA, EMA, MHRA, ANSM, BfArM, AGES and other DRAs in Europe) is accepted
  - The scope is expanded to also include BE Inspection Reports in which the products researched in the BE studies are similar to the product submitted for registration
  - This expansion of scope is applicable for all BE study centre including BE study centre in countries besides United States, Canada and Europe
  - Effective date **1 July 2016**

Regulatory Updates – 6 (..cont)

- New requirement for Option 2 Process Validation in new pharmaceutical product and variation application:
  - According to the ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration, there are new requirements for companies who select Option 2 in submission of process validation report:

Regulatory Updates – 6 (..cont)

- Option 2:
  - PRH also need to ensure the following are fulfilled:
    - Pharmaceutical Product Development Report
    - Validation data for 1 pilot batch along with validation scheme for commercial batch
    - Letter of commitment to ensure that company will only market the product after the satisfactory c
    - Complete Process Validation Study Report for 3 consecutive commercial batches must be submitted within 1 year from the registration date
    - Complete and satisfactory information or data must be submitted within 6 months from the submission date of the Validation Study Report date

Regulatory Updates – 6

- New requirement for Option 2 Process Validation in new pharmaceutical product and variation application:
- Option 2 is allowed for pharmaceutical products in the dosage forms of injection and modified release. It is **not allowed** for biologic/biotechnological products

Regulatory Updates – 7

- Malaysian Variation Guideline for Natural (Traditional Medicine & Homeopathy) & Health Supplement Products (Abridged Evaluation)
  - There are **37** types of variation listed in the Guideline
    - 13 Major Variation (MaV)
    - 16 Minor Variation – Prior Approval (Miv-Pa)
    - 8 Minor Variation – Notification (MiV –N)
  - Effective **1 August 2016**

Regulatory Updates – 8

- Directive on Requirement to the GLP for Non-Clinical Safety Studies for the Registration of New Chemical Entity (NCE), Biologics and Herbal with High Therapeutics Claim
  - All non clinical safety studies submitted for registration of products involving New Chemical Entity (NCE), biologics and herbal with high therapeutics claim must be conducted under GLP
  - A Final Report must be provided for each of the non clinical safety studies conducted
  - Effective date **1 January 2018**

Regulatory Updates – 9

- Directive on Plasma Lot Release on All Plasma Products Registered in Malaysia
  - Approved by DCA in June 2016 Meeting
  - PRH is responsible to have a contingency plan to ensure the supply of plasma products in Malaysia is not affected if the product do not fulfil the requirement of Plasma Lot Release in Malaysia
  - Effective date **1 July 2016**

Regulatory Updates – 10

- Cell and Gene Therapy Products (CGTPs)
  - Guidelines and Framework approved by DCA in January 2016
  - Guidelines uploaded on NPRA Website
  - Effective **1 January 2021**
  - Transition period:
    - Voluntary Registration – only registered CGTPs can be used for therapy
    - Status Quo – only for research purposes, with CTIL/CTX from BPFK
  - Circular: 10 March 2016

Regulatory Updates – 11

- Directive on Requirement of Foreign GMP Inspection for the Purpose of Registration/ Renewal of Pharmaceutical Products.

(Note: to be share in other session)

Regulatory Updates – 12.1

New QUEST3+

Features	Details
Payment mode	2 types of online payment : i)Internet banking via Financial Process Exchange (FPX) ii)Credit Card via MasterCard Internet Gateway Service (MiGS)
Others	Limited number of correspondences Milestones for Correspondences/Replies

Regulatory Updates – 12.2

New QUEST3+

Modules	New Features
Product Registration	1. Screening process in the evaluation work flow 2. Information for API based on active substance and manufacturer
Licensing	Application for Manufacturing, Import and Wholesale Licencethrough online system
Quality Control	Screening process in the protocol & validation evaluation work flow
Cosmetic	Additional information in attachment format for :- 1. Product Label 2. Letter of Authorisation include Letter of Contract Manufacturing Appointment and Acceptance

Regulatory Updates – 13

- HALAL Certification for pharmaceutical products.

Halal logo from JAKIM are allowed on the label for;

- Cosmetics,
- Herbal/Traditional products,
- Non prescription products, (except parenterals)

Halal logo from JAKIM are NOT ALLOWED on the label for;

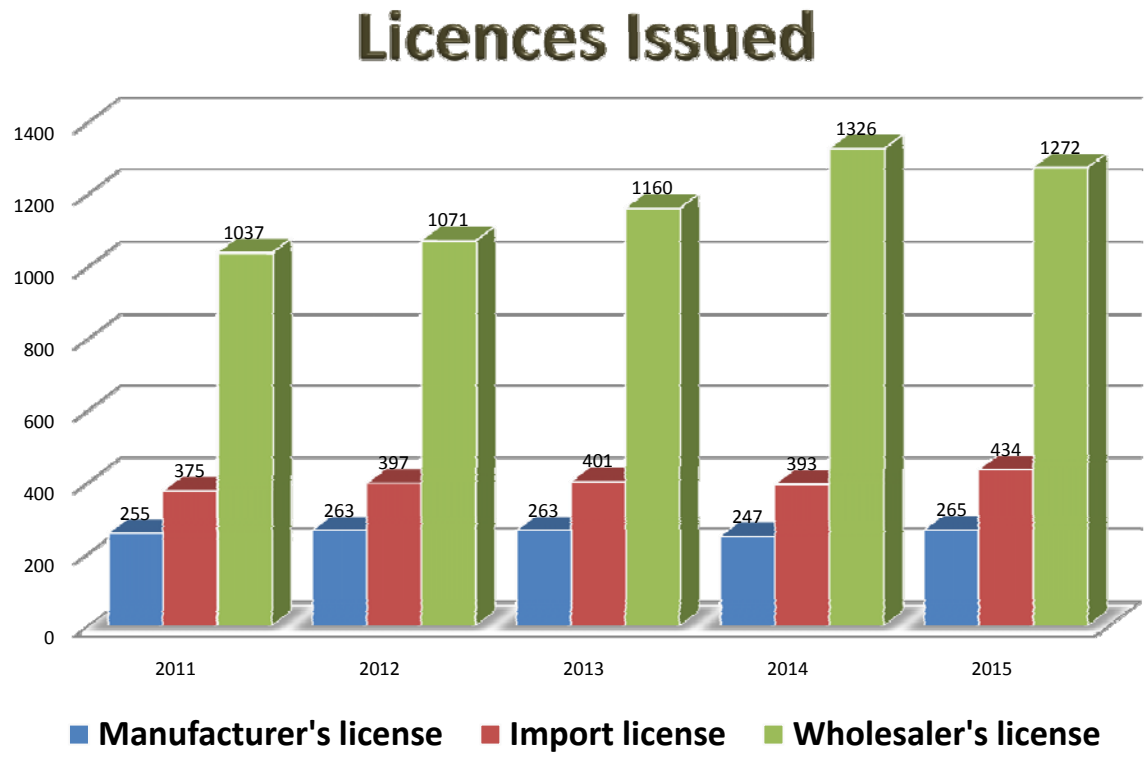
- Prescription products,
- Veterinary medicines,

Product Registration status (as Dec. 2015)

Product Category	Total
Prescription Products	6,833
Non Rx (OTC) Products	4,094
Herbal/Traditional Medicines	11,896
Med. Veterinary Products	515
Health Supplements	692
TOTAL	**24,030**
Cosmetics**	85,000

*Source: NPRA

Licensed Premise (as Dec. 2015)



*Source: NPRA

More info….

http://npra.moh.gov.my