Regulatory Updates (NRC 2013)

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WHO Collaborating Centre for Regulatory Control of Pharmaceuticals

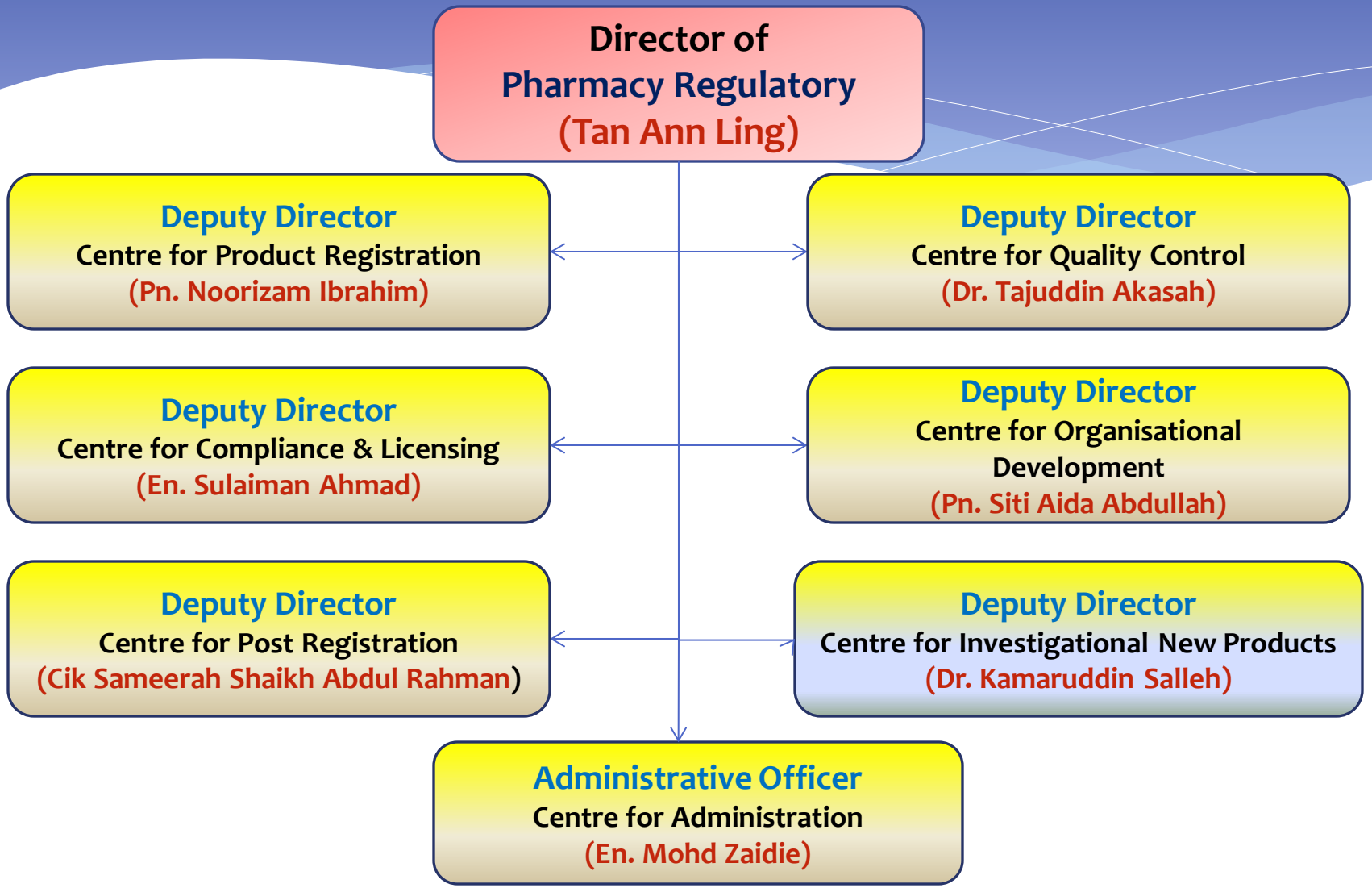
Member of Pharmaceutical Inspection Co-operation Scheme

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

OVERVIEW

- NPCB Organisation Chart/Heads of Centre
- NPCB New Mission & Vision Statements
- Major Milestones
- Regulatory Updates
- Way Forward
- Future Plans

NPCB ORGANISATION CHART



NPCB's PREVIOUS VISION & MISSION STATEMENT

VISION

The National Pharmaceutical Control Bureau will be a centre of excellence on pharmaceutical regulatory matters to ensure the health and well-being of mankind

MISSION

The National Pharmaceutical Control Bureau shall ensure the quality, efficacy and safety of pharmaceutical products through the implementation of relevant legislation by a competent workforce working together in strategic alliance towards improving the health of the people

NPCB's REVISED VISION & MISSION STATEMENT

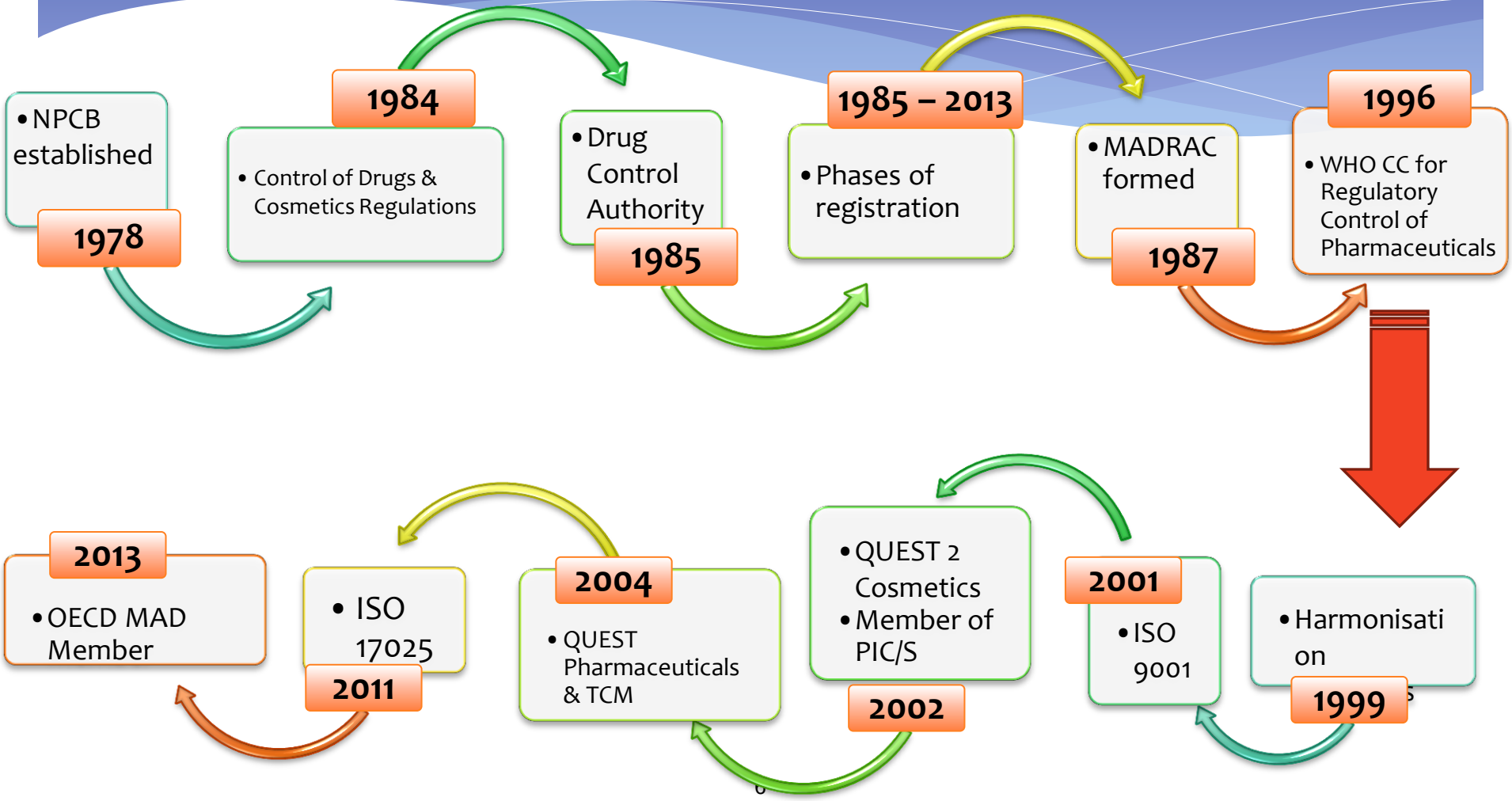
VISION

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

MISSION

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

NPCB: MILESTONES



MALAYSIA's MEMBERSHIP IN OECD MAD

29 March 2013

NPCB as the Compliance Monitoring Authority (CMA) for :

- ✓ Pharmaceuticals (includes vaccines, natural product and biologics)
- ✓ Cosmetics
- ✓ Food additives
- ✓ Veterinary drugs

Malaysia became full adherent member to OECD MAD in the Assessment of Chemicals:

- ✓ Non-clinical safety data related to the protection on man and its environment will be accepted by OECD.

STANDARDS MALAYSIA as the Compliance Monitoring Authority (CMA) for :

- ✓ Pesticides
- ✓ Non-Pharmaceutical Biotechnology Products
- ✓ Animal Feed & Additives
- ✓ Chemicals

REGULATORY UPDATES: DATA EXCLUSIVITY (DE)

- Directive on DE effective as of **1st March 2011**
  - **New Chemical Entities (NCE)**
    - Application within 18 months from date of first registration
    - Duration: 5 years granting of DE in country of origin
  - **Second Indication** of registered products.
    - Application within 12 months from approval of second indication
    - Duration: 3 years
  - Granted by Senior Director of Pharmaceutical Services, MOH
  - Exclusion: Compulsory Licensing, National Emergency etc
  - Not applicable to Biologics/Biotechnology Products

REGULATORY UPDATES : ACTIVE PHARMACEUTICAL INGREDIENTS (API)

- API requirements for new drug applications was implemented in stages:
  - **New Chemical Entities (NCE)**
    - April 2011 : Voluntary
    - January 2012 : Mandatory
  - **Generics :** In stages according to risk
    - Injectables/Parenterals : Tentative January 2014
    - Others: To be decided
- **Other issues:**
  - Existing Products: To be decided
  - GMP Standards: PIC/S, WHO,

REGULATORY UPDATES : BIOEQUIVALENCE (BE)

- Implementation of requirement for BE studies for all **generic "Immediate Release, Oral, Solid Dosage Form"** products
  - Extension to previous 9 lists
  - Applicable only to products containing **Scheduled Poisons**
    - New Registration : 1st January 2012
    - Existing Products: 1st January 2014 upon submission for renewal
- Accreditation of BE Providers/Centres
  - Inspections by NPCB auditors based on GCP and GLP Principals
  - Local and Foreign Centres
  - Payment by Product Holder – Inspection fee for foreign inspections (€5,000 + Expenses)
  - Listing of approved BE Centres in NPCB website

REGULATORY UPDATES : BIOEQUIVALENCE (BE)

- Notification of BE studies conducted in **Local or Foreign** BE Centres for Registered or to be Registered Products
  - Effective 1 January 2012
  - Local BE Centres that do not require CTIL/CTX
    - Local Pharmaceutical Manufacturer
    - Foreign Pharmaceutical Manufacturer
  - Foreign BE Centres accredited/recognised by NPCB
    - Local Pharmaceutical Manufacturer
    - Exempted for Foreign Pharmaceutical Manufacturer
      - Documents required during registration
      - Inspection report valid for 3 years after inspection

REGULATORY UPDATES : BIOEQUIVALENCE (BE)

- Biopharmaceuticals Classification System (BCS) based Biowaiver
  - Immediate Release Oral Dosage Forms Generics
    - API in BCS Class I (High Solubility & High Permeability Rapid Dissolution & Absorption)
- Revisiting Policy on BE Requirements
  - New Comparators
  - Possible exemptions for Grandfather Products
    - Formation of task force
    - Possibly based on individual API and not time-based

REGULATORY UPDATES : GOOD MANUFACTURING PRACTICE (GMP)

- Pharmaceutical products from foreign countries must be manufactured in a PIC/S or ICH country

OR

- facility that has been inspected and compliant to PIC/S GMP guidelines by a National Drug Regulatory Agency of a PIC/S or ICH Member Country

OR

- ASEAN Member State listed in ASEAN Sectoral Mutual Recognition Arrangement for GMP

Implementation date:

- **1st July 2012 : new registration of pharmaceutical products**
- **1st January 2014 : product registration renewal**

REGULATORY UPDATES : GOOD MANUFACTURING PRACTICE (GMP)

- Reason for Implementation
  - Equalised GMP Standard used – Local & Imported
  - Safeguard Patients Safety – Ensure High Quality Products
  - Level Playing Field for Local & Foreign Manufacturers
- Exemption Clause
  - Unmet Medical Needs – Orphan Drugs
  - Life-Saving Products – Oncology/Anti-Retrovirus
  - National Emergency – Pandemic
  - Technology Transfer

REGULATORY UPDATES : GOOD MANUFACTURING PRACTICE (GMP)

- Revisit Current Directive on PIC/S GMP
  - Exemption Clause
  - GMP inspection of Overseas Facilities by NPCB
    - First refusal
    - Extension to other category of products when necessary
      - API, Health Supplement, Tradisional/Herbal
- Enforcement on Traditional Manufacturing Facilities
  - Water Treatment System : 1st July 2013
  - Centralised Air Handling System: 1st January 2014
  - Prohibition from manufacturing food in licensed traditional facilities: February 2013

GMP Scope Expansion

* Blood establishments
  - Fractionation
  - Collection centres
* Biologicals
  - Cellular & Genetic Therapy Products (CGTPs)
* API
  - Pharmaceuticals
  - Herbals
* Healthcare establishments
  * hospital clean room facilities
* Nuclear pharmacy/ radiopharmaceuticals
* Compounding Facilities
  - TPN

REGULATORY UPDATES: STABILITY STUDY

- Long Term Stability Study – Prescription & OTC
  - ICH Zone 4B : 30°C ± 2°C , 75% RH ± 5%
  - New registration : Effective 2009
  - Existing as of 2009: Data upon renewal
    - Variation – Labeling on storage condition
- Exemption
  - API not Stable at Zone 4B - Justification
  - Products requiring Cold Chain
- Deadline: 1st January 2015

REGULATORY UPDATES: FOOD DRUG INTERPHASE (FDI)

- Classification by NPCB as of 1st January 2013
  - Classification tree available on website
- Existing Products as of December 2012
  - Can be marketed until 31st December 2013
- New Products
  - Must be registered
- Products containing Gamat (*stichopus spp*) taken orally must be registered
- Products in pharmaceutical dosage forms
  - Cannot be classified as food

REGULATORY UPDATES: VARIATION

- Malaysian Variation Guidelines (MVG)
  - Based on ASEAN Variation Guidelines adopted by ASEAN in July 2012 and come in force in July 2013
  - Certain Country Specific Requirements
  - Implementation:
    - 1st July 2013 – Minor Variation Notification (MiV-N)
    - 1st January 2014
      - Conditions & documentations for Major Variation (MaV) & Minor Variation – Prior Approval (MiV-PA)
      - Grace period for implementation by PRH after approval of variation

REGULATORY UPDATES: SECURITY HOLOGRAM

- Also known as Meditag
- Purchased only by Manufacturers & Importers licensed by DCA
- Requirements:
  - Maintain Security Hologram Register – usage, reconciliation, batch No., Serial No., Name of Product, etc
  - Attached to immediate packaging
  - Cannot be transferred or sold to 3rd party
    - Own products only
  - Subjected to audit
- Complaints – Diversion, reuse etc

REGULATORY UPDATES: HALAL LOGO

- Halal Logo previously allowed:
  - Cosmetics
  - Traditional/Natural Products
  - Health Supplements
- As of 1st January 2013, allowed for OTC Products except parenteral
- Voluntary - Approval by JAKIM & Islamic Bodies recognised by JAKIM
- Declaration on label if contain any ingredient from animal source eg porcine, bovine

REGULATORY UPDATES: CONSUMER MEDICATION INFORMATION LEAFLET (RiMUP)

- Required for **ALL** Products that are self-administered by patients
- Effective on 31st December
  - 2011 : Diabetes & Hypertension
  - 2012: Cardio-vascular, Chronic Respiratory Disease, Psychiatry, Chronic Renal Disease, Epilepsy, Osteoporosis
  - 2013: Other Scheduled poisons, OTC, THMS with high claims
- Submission Check list & Standard Format available
- Upload on NPCB Web-site

REGULATORY UPDATES: HIGH/MEDIUM CLAIMS FORHEALTH SUPPLEMENTS (HS)

- Registration of HS with effect 1st March 2013
  - General Claims
    - General Health Maintenance
  - Functional Claims (Medium)
    - Maintains or enhances the structure or function of the human body, excluding disease-related claims
      - Standard Reference/Scientific evidence from human observational studies
  - Disease Risk Reduction Claims (High)
    - Significantly altering or reducing a risk factor of a disease or health related condition
      - Human intervention study, toxicology (chronic) & Pharmacology Studies [23]

REGULATORY UPDATES: CHANGE OF PRODUCT REGISTRATION HOLDER (PRH)

- Product Owner has full rights over product
- PRH has rights over the registration of product
  - Change of PRH can only be done by present PRH
- No agreement bet. Owner & PRH for Change
  - Products deregistered upon receipt of letter of termination from Product Owner
- Fast Track Registration possible
- Effective 3 April 2013

REGULATORY UPDATES: MISCELLANEOUS

- Product Registration Holder (PRH) instead of Market Authorisation Holder (MAH)
- Licensing of Veterinary Products – July 2013
- Abolishment of Product Registration Certificate (SPP) as of 1st February 2013
- Requirement for Certificate of Analysis for every batch of registered product imported to be kept as of January 2013

REGULATORY UPDATES: MISCELLANEOUS

- Exemption of patient dispensing pack for certain cream/ointment ⟹ *Effective December 2010*
  - Hospital use and Skin Specialist clinic only
  - Limit to certain types
    - Weak & moderately potent corticosteroids
    - Emollients and Protectives – Max: 500gm
    - Wounds & Ulcers – Max: 500ml – 1 liter
    - Antipsoriatics - Max 500ml/gm

Strengthening ADR

* Increase ADR reporting
  * Target > 50% WHO standard
  * AEFI reporting for all vaccines
  * Reporting by private health professionals & consumers
  * Reporting by consumers
  * On-line reporting via website
* Risk Minimization & Risk Communication
  * Pharmacovigilance Committee
  * Patient Information Leaflets (RiMUP)
  * Drug Safety News (REAKSI)

Business Process Reengineering

- Licensing process reduce from 10 to 4 working days effective 1 Jan 2012
- Changes in registration flow processes
  - Incorporating screening process
- New Client Charter
- Support development of local pharmaceutical industry
  - Rural Transformation Centres (NBOS)
  - Halal pharmaceuticals
  - NKEA : Healthcare
    - EPP2 : Clinical Trials
    - EPP3 : Malaysian Pharmaceuticals
  - NKEA : Agricultural
    - EPP1 : High Value Herbal Products

FUTURE POLICIES: NEW REGISTRATION PROCESS

- Development in line with QUEST 3+
  - Specification approved
  - Restricted Tender
- Limit No. Of Correspondence
- Fixed Timelines for Evaluation & Response
- Rejection of Application at Multiple Levels

FUTURE POLICIES: LIST OF CERTIFIED LABORATORIES

- Testing of TM/Natural Products
  - Mandatory testing of every batch produced
  - Requirement of CoA for every batch imported
  - Acceptance of CoA from Certified Lab. for purpose of Registration
- Criteria
  - SAMM Accredited in required scope (MS ISO 17025)
  - Valid Contract between Manufacture/PRH
  - Audited by NPCB
- Voluntary ⇒ List uploaded in NPCB website

FUTURE POLICIES: ANIMAL FEED & PREMIXES

- Malaysia Animal Feed Act 2009 (Act 698)
  - Published in Gazette on 3 September 2009
  - Enforced in April 2013
  - Does not extend to Sabah & Sarawak
- Hand over regulatory control of Animal Feed Additives/Premixes to DVS
  - Redundant as already controlled under this Act
  - Additives containing Scheduled Poison
    - Poisons Act 1952 – Poisons A Licence

FUTURE POLICIES: REGULATING CELLULAR & GENETIC THERAPY PRODUCTS (CGTPs)

- Formerly known as ATMPs or ATPs
  - Consist of Gene Therapy, Cell Therapy and Tissue Engineered Products
- NPCB - authority body in the regulatory control of CGTPs
  - Registration of CGTPs used for medicinal purposes
  - Licensing of facilities – GMP/GDP/GTP Requirements
    - Manufacturing
    - Storage
    - Practice

FUTURE POLICIES: REGULATING CELLULAR & GENETIC THERAPY PRODUCTS (CGTPs)

- Formation of TWG for CGTP on September 2012
  - Development of the regulatory framework of CGTPs
    - Definition
    - Criteria for Product Classification
    - Organisation of Application Dossier
    - Requirement for Quality Control
    - Clinical & Non-Clinical Requirements
    - Risk Management/Post Registration
    - Proposed Timeline: **4th Quarter 2013**
  - Consist of
    - Agencies under the Ministry of Health Malaysia
    - Academicians involved in cell research
    - Private sector

FUTURE POLICIES: REGULATING CELLULAR & GENETIC THERAPY PRODUCTS (CGTPs)

- Similar approach as USFDA - Products classified:
  - Class 1 – Do not require registration
    - Minimally manipulated
    - Homologous use only
    - Not combined with drug, device or biologics
    - Does not have systemic effect with certain exemptions
  - Class 2a – Require registration
    - Established cell therapies
    - Abbreviated data/documentation
  - Class 2b - Require registration
    - Novel Cell and Gene Therapies
    - Complete Chemistry, Manufacturing and Controls (CMC)

WAY FORWARD: REVIEW WORK PROCESSES

- Risk Based Approach to:
  - GMP Certification
  - Quality Control Testing
  - Post Market Surveillance
  - Research & Development
- Upgrading of Testing Facilities for Biologics
  - Lot Release of Imported Vaccines including laboratory testing
  - Quality control testing of Biosimilars eg EPO

WAY FORWARD: INTERNATIONAL COLLABORATION

- Greater Focus on Collaboration with other NDRAs
  - MoU with HSA, Singapore – signed March 2012
  - Discussion/Talks with
    - SwissMedic
    - NADFC, Indonesia
    - KFDA
  - Joint GMP Audits
  - Joint/Collaboration - Evaluation of Dossiers
  - Shared Resources/Expertise

THANK YOU

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