REGULATORY FRAMEWORK FOR MEDICAL DEVICES CONTAINING MEDICINAL PRODUCTS

Dr. Rama Sethuraman, Senior Manager, Medical Devices Branch, Health Science Authority, Singapore
Scope

• Regulations in Singapore
  – Product Classification
  – Pre-market Overview
  – Post-market Controls

• Similarities/Differences from other countries

• ASEAN updates
Medical Device Combinations

- Combination of two or more health products from different categories in a single product to achieve the intended purpose.
  - Medical Device + Drugs
    e.g. Sirolimus eluting Stent, Pre-filled Syringe containing insulin
  - Medical Device + Biologics
    e.g. Bone void fillers containing Bone morphogenic protein
  - Cell Tissue Therapy Products + Medical Device
    e.g. Membrane patch containing Duramater cells for use in spinal/ neurosurgery
Why combine?

• Extend the lifecycle of off-patent medicinal products
• Improve the effectiveness of medical devices by adding medicinal substances
• Generating new market value for current products that will soon lose patent
• Consumer interest in localized drug delivery - improved therapeutic effectiveness
General Scope

• A product comprised of a medical device and one or more health product(s) (e.g. Drug, biologics) that are combined together and produced as a single entity;
  (e.g. Drug eluting stents, Pre-filled syringes with medicinal products)

• A medical device and one or more health product(s) supplied together but as distinct entities and intended to be combined at the point of administration or used together to achieve a common intended purpose
  (e.g. Hemostatic device & Thrombin, Insulin pen & Insulin)

• A medical device and one or more health product(s) supplied together but as distinct entities although not intended to be combined at the point of administration or used together
  (e.g. Procedure packs, First aid kits with lidocaine vials)
Understanding the Possibilities

• Combined together as a single entity
  e.g. Drug eluting stents
  Drug in Pre-filled syringes

• Supplied together AND
  • Combined together at point of administration OR
  • Used together for a common intended purpose
    e.g. Hemostat device & Thrombin

Drug + Device

• Supplied together BUT
• Used individually AND
  • No common intended purpose
  e.g. First aid kit with Drug
Combination of Device and Drug include
• Two Constituent Components
• Two Modes of Action

**MODE OF ACTION**
• Identify the PRIMARY and ANCILLARY Mode of Action

Primary Mode of Action (PMOA) $\rightarrow$ makes the greatest contribution to the overall intended therapeutic purpose of the product

Ancillary Mode of Action $\rightarrow$ plays a supporting role in the overall intended therapeutic purpose of the product

PMOA determines the regulatory control applicable to the product.
Risk Classification

- **Class D Medical Device**
  - Rule 13 of GN-15 *Guidance on Risk Classification of General Medical Devices*
  - Devices incorporating a medicinal product
Evaluation Routes

• Two Routes of Evaluation

1. ABRIDGED – applicable only if

   (i) Product is approved as medical device in one Reference Agency* and
   (ii) the drug or biologics component evaluated and approved by at least one competent drug regulatory agency, as defined by the WHO

2. FULL - For all devices that do not qualify for abridged route

Reference agencies (GHTF Founding Members):
A well-established medicinal product coated on an approved medical device

The intended use and/or indications of a medicinal product incorporated in a medical device may differ from its approved use as a medicinal product by itself.

**Paclitaxel**
Cancer Chemotherapy

**PTCA Balloon Catheter**

**Paclitaxel-coated PTCA Catheter**
Paclitaxel intended to prevent proliferation of Smooth muscle cells in Vascular tissue

**Intended Use and Indications Differ**
Combination – concerns

- Presence of a polymer coating system – a matrix that assists coating of the medicinal product to the stent surface
  - Compatibility issues
  - Mechanical attributes
  - Stability

- Non-conventional release profile of the medicinal product
  - Local release vs. systemic effect

- Synergistic effects of the components put together in the combination

- New route of administration and new delivery system
Advantages

• Identifying the risks and hazards associated with a medical device
• An effective form of regulatory oversight in the absence of pre-market approvals or product registration system
• Enables timely intervention by Regulatory Authority to safeguard public health

Important Learning Points

• All medical devices possess inherent risk, regardless of risk class
• Limitations of premarketing assessment in terms of long-term safety & effectiveness
Post-market Controls

Reporting and investigation of adverse events and field safety corrective actions

- Mandatory reporting by Registrants & Dealers
- Voluntary reporting by Healthcare professionals & consumers

Post-Market VIGILANCE

Pro-active collection of information on quality, safety or performance of medical devices after they have been placed in the market.

- Active Environmental Scanning
  - Subscription to overseas alerts from overseas regulatory authorities
  - Review overseas Field Safety Notice publications

Post-Market SURVEILLANCE
Regulation of combinations based on main function/purpose

Use of Standards in Pre-market review

Singapore MD Regulatory Framework

Lead Agency for review – based on Primary Mode of Action
Pre-market Review and Requirements - FDA guidance documents

Regulation of combinations based on main function/purpose
Grouping for Device Licence
(Single, Family, Group, Group Family, System & Test Kit)

Risk Classification system for Medical Devices
Essential Requirements Checklist for Medical Devices

Risk Classification system for Medical Devices
Post-market – Recall and Adverse Event reporting
Essential Requirements Checklist for Medical Devices

Regulation of combinations based on main function/purpose
Use of Standards in Pre-market review
Medical Device Product Working Group (ASEAN ACCSQ-MDPWG)

Formed in 2005 by Medical Device Regulators in ASEAN

• Chair: Malaysia
• Co-Chair: Singapore

Objective:

To implement specific measures on medical device under the roadmap for healthcare integration, in-line with the establishment of the ASEAN Economic Community (AEC) by the year 2020 and fast-track integration of the 11 priority sectors (including healthcare sector).
ACCSQ MDPWG Agenda

- Harmonised Regulatory Framework: ASEAN MEDICAL DEVICE DIRECTIVE (AMDD)
- Harmonised pre-market submission format: Adoption of ASEAN CSDT
- Harmonised set of voluntary medical device standards in ASEAN
- Sharing of post-market safety information among ASEAN Member States
Thank You