Singapore’s Post-market Surveillance System
Lessons learnt & challenges identified

WHO Global Forum on Medical Devices
Bangkok, Thailand

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9 September 2010
Singapore

- **Geographical location**: 1° N of equator
- **Total land area**: 710 sq km
- **Population**: approx 5 mil
Singapore

- People: Chinese (77%), Malay (14%), Indian (8%), Others (1%)
- Infant mortality rate: 2.1 per 1,000 live births
- Av. life expectancy rate: 80.6 yrs
- Leading causes of mortality: Cancer, IHD, pneumonia

(61.4% of total deaths in 2007)

Source: MOH Website
Association of Southeast Asian Nations (ASEAN)

ACCSQ-MDPWG
Chair: Malaysia
Co-Chair: Singapore
Asian Harmonization Working Party

Member Economies:
- Abu Dhabi
- Brunei Darussalam
- Cambodia
- Chinese Taipei
- Hong Kong SAR, China
- India
- Indonesia
- Kingdom of Saudi Arabia
- Korea
- Laos
- Malaysia
- Myanmar
- People's Republic of China
- Philippines
- Singapore
- South Africa
- Thailand
- Vietnam

Chair: China
Vice-Chair: India
TC Chair: Singapore
Co Chairs: Saudi Arabia/Chinese Taipei
Global Harmonization Task Force

An international forum for medical device regulators and medical device trade associations

Objective: To develop harmonised principles relating to the regulation of medical devices
Overview

1. Implementation Milestone

2. Post Market Activities ‘pre-implementation’ of HPA

3. Post Market Activities ‘post-implementation’ of HPA
   • Adverse Event Reporting
   • Field Safety Corrective Action / Recall Reporting

4. Challenges
Medical Device Branch, HSA

• **Mission:**

  To safeguard public health by ensuring that the medical devices supplied in Singapore are safe, of good quality, and able to meet their intended use/s

• **Oversight:**

  Premarket - registration
  
  Post market – FSCA & AEs
  
  Clinical trials – MD & Clinical Trial Branch

• **Manpower:**

  20 professional staff, 4 support officers
Implementation Milestones

Health Products Act

**Phase 1: Post-market Duties**
(e.g. keep supply records, report adverse events and FSCAs)

**Phase 2: Accept Product Registration and Licence applications**

**Phase 3A:**
- Mandatory PRODUCT Registration of Class C&D
- Mandatory licensing of Dealers

**Phase 3B: FULL IMPLEMENTATION**
Mandatory PRODUCT Registration of Class A & B

**Voluntary Product Registration (VPR)**

1 Nov 2007
1 Nov 2008
10 Aug 2010
1 Jan 2012
Purpose of Post Market System

Advantages

• Understanding 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

• All medical devices possesses inherent risk, regardless of risk class

• Limitations of premarketing assessment & development criteria
Medical Device Branch, HSA

• Mission:
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What is a Field Safety Corrective Action (FSCA)?

Examples

1. **Product Recall** (e.g. Recall of specific lots of catheters due to possible breach of sterile packaging)

2. **Device modification** (e.g. Modification to C-arm component of X-ray Diagnostic System to prevent unintentional movements of C-arm during procedure which can cause injury to patient)

3. **Software upgrade** (e.g. Software upgrade to correct ventricular sensing anomaly in Implantable Cardioverter Defibrillator)

4. **Addendum to Instructions for Use (IFU) related to safety** (e.g. Additional warning added to IFU to inform consignees of possible failure mode of action)

5. **Information on clinical management of patients** (e.g. Advice to Surgeons on patient management of patients with implants that have been subjected to a recall)
What is an Adverse Event (AE)?

Examples

1. **Death to patient** (e.g. Balloon catheter fails to deflate and patient death results)

2. **Serious injury to patient** (e.g. Hospital bed railing collapses and patient falls down and fracture hip)

3. **No death or serious injury to patient but if AE recurs, death or serious injury to patient occurs** (e.g. Failure code occurs in infusion pump which causes pump to stop infusing however, nurse who was present, attends to rectify device malfunction)
MD Post market vigilance in Singapore

Capitalise & leverage on existing strengths:

- International collaboration
  - TGA, MHRA, BfArM, US FDA, Heath Canada, Swiss Medic

- Ability to respond swiftly to safety concerns

- Good networking with HCPs, Healthcare Institutions & researchers
Before 1 Nov 2007

1. Voluntary reporting from industry members

2. Active Environmental Scanning
   - Subscription to overseas alerts from overseas regulatory authorities
     - US Food Drug Administration (FDA)
     - UK Medicines and Healthcare products Regulatory Agency (MHRA)
     - Health Canada
     - Swiss Medic
   - Review Field Safety Notice overseas publications
     - Germany Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)
     - Australia Therapeutic Goods Administration
   - Other forms of publications
Before 1 Nov 2007

Challenges
• Lack of information
  • on availability of affected products in local market
  • on distributor of affected products in local market
• Lack of reporting initiative from industry members

Lessons learnt
• Market survey of available MDs in the market and issues associated with these MDs
• Create awareness for both users and dealers of MDs
• Education and preparation for upcoming regulatory requirements
• Timely intervention to safeguard public health
1 November 2007

Post-market duties commenced on 1 Nov 2007, and all dealers of medical devices are required to:

• maintain records of import and supply
• maintain records of complaints
• report adverse events to HSA
• notify HSA concerning product recalls and field safety corrective actions
• prohibition against false or misleading advertisement
Life cycle approach to safety monitoring for Medical Devices

Process

- Risk detection: Monitoring AEs & safety signals
- Risk assessment: Assessing risk-benefit profile
- Risk minimisation: Minimising risk by appropriate regulatory actions
- Risk communication: Communicating information to optimise safe & effective use
Adverse Event (AE) reporting

What are Reportable Adverse Events?

Any adverse event (AE), which meets the three basic reporting criteria listed below, is considered as a reportable AE. The criteria are that:-

• an AE has occurred;

• the medical device is associated with the AE;

• the AE led to one of the following outcomes;
  ➢ a serious threat to public health;
  ➢ death of a patient, user or other person;
  ➢ serious deterioration in state of health, user or other person;
  ➢ no death or serious injury occurred but the event might lead to death or serious injury of a patient, user or other person if the event recurs.
Reporting Channels

Mail
Fax
Tel
Email to HSA_md_info@hsa.gov.sg
Online reporting
Recall & FSCA reporting

Recall

An action taken by a product owner to remove the health product from the market or to retrieve the health product from the market because the health product:-

• may be hazardous to health;
• may fail to conform to any claim made by its product owner relating to its quality, safety or efficacy.

Field Safety Corrective Action (FSCA)

An action taken by a product owner to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device. This may include:-

• the return of a medical device to the product owner or its representative;
• device modification;
• device exchange;
• device destruction;
• advice given by product owner regarding the use of the device.
Recall & FSCA

FSCA
Recalls

To be the LEADING INNOVATIVE AUTHORITY
protecting and advancing NATIONAL HEALTH and SAFETY
All Rights Reserved Health Sciences Authority
Device categories affected:
• Defibrillators
• Catheters
• Orthopedic implants
• Surgical instruments
• Stretchers
• Wheelchairs
• X-ray/CT system
• Ultrasound system
• Infusion pumps
• Hot cold gel packs
• Contact lenses
• In-vitro diagnostic devices

No. of FSCAs in Singapore Between Nov 2007 to Jul 2010

Recalls 269

Other Corrective Actions 535
Risk communication

Aim:

To enhance safe use & minimise risks of devices

To update & inform intended audience of safety issues in a timely, transparent & unbiased manner
Risk communication

- Press releases
- Dear Healthcare Professional Letters
  (via conventional mail, e-mail, SMSes, faxes)
- Updates on HSA website, MOH healthcare professional portal**
- ADR News bulletin
- Manning of hot-lines during crisis
- Handling of media queries
Dear Healthcare Professional

Public advisories (website, press, TV)

Letters

SafetY information

Dear Healthcare Professional

HSA's Expert Advisory Committee's Recommendations

The Health Sciences Authority has convened an expert advisory committee to review the risk-benefit balance of COX-2 selective and non-selective NSAIDs. The Committee comprised 11 experts representing relevant specialties and expertise, viz. rheumatology, cardiology, gastroenterology, colorectal surgery, pharmacology, orthopaedic surgery, family medicine, dermatology, pharmacy and pharmacovigilance (see Annex 1).

Background information

The degree of COX-2 selectivity of COX-2 selective NSAIDs has not been definitively established as there is considerable overlap with the other NSAIDs when assessed by different in vitro assay techniques. Commonly known COX-2 selective NSAIDs include drugs such as celecoxib, etoricoxib, rofecoxib and valdecoxib. However, based on the findings of in vitro tests, some of the older NSAIDs such as diclofenac, meloxicam and nimesulide have also shown to have more COX-2 selectivity compared to other NSAIDs such as ibuprofen, ketoprofen, ketobucel, mefenamic acid, naproxen and piroxicam.

Conclusion on the risk-benefit assessment of COX-2 selective and non-selective
Protocol for Recalls

- Background of FSCA/AE
- Investigations conducted by HSA
- Action plan formulated by HSA
Post Market Implementation

Learning Points

• Importance of strong regulatory & scientific network and professional collaborations

• Limitations of premarketing assessment & development criteria

• Highlights importance of post marketing surveillance
Improvements to post market system

• Merits of running an **online system** (email instead of hardcopy fax). Plans in place to move to online reporting in 2010.

• Educate industry on regulatory requirements of FSCA reporting better. Help **foster understanding** on regulatory requirements and improves regulatory submissions.
Challenges

• Lack of reporting initiative from industry members at the initial phase

• Distributor no longer in existence, resulting in devices that are not corrected

• Reporting information deficient or inaccurate

• Lack of traceability of devices by distributors

• Compliance issues

• Changing the mindset of industry members
  - “my device is safe”
  - “my device is of very low risk”
Future Post Market Challenges

• Opportunities in genomic era
• Registries for implants & gene therapy
• Maximising IT tools for signal detection & communication
• Forging closer ties with international counterparts
Thank You
Case Studies
Case Study 1 – Hot/Cold Gel Packs

Background

September 2008: HSA received a recall report from an Australian company

Intended use of hot/cold gel packs: Compress to relieve pain (can be frozen for cold therapy or heated in the microwave for heat therapy)

Issue

Reason for recall: Case of accidental poisoning of a young child, following ingestion of contents of a brand of hot cold pack, in Australia.

Subsequent TGA testing found several brands of cold hot packs to contain the toxic substance ethylene glycol* (rather than the non-toxic propylene glycol).

* Ethylene glycol is harmful or fatal if swallowed and may also cause allergic skin reaction, irritation to skin, eyes, and the respiratory tract.
**Case Study 1 – Hot/Cold Gel Packs**

**HSA’s Investigations**

- This prompted HSA’s investigation of all brands of hot/cold packs available in Singapore.

- HSA conducted laboratory tests on product samples of 7 available brands, and found that 3 brands carried products that contained ethylene glycol. The other 4 brands carried hot/cold packs containing the non-toxic substance, propylene glycol, as the anti-freeze ingredient.

- Over 2000 affected devices have been sold to consumers since 2006.
Case Study 1 – Hot/Cold Gel Packs

**HSA’s Action Plan**

- Upon confirmation of the affected devices, the respective distributors and manufacturers are informed and instructed not to import, export or sell the affected hot/cold packs.

- A public press release was issued for the consumer level recall. The distributors and manufacturers of the hot/cold pack were also instructed to do a public notification on the recall.

- Distributors are instructed to provide monthly updates to HSA regarding the status of the recall for the duration of this consumer recall.

- Upon closure of the recall, the distributors were instructed to destroy all the affected hot/cold packs.

- Manufacturers are required to provide COA demonstrating that the hot/cold gel packs, intended for supply in the Singapore market, do not contain ethylene glycol.

- Additional labeling and product specific requirements for hot/cold gel packs containing trace amount of ethylene glycol.
Case Study 2 – B.C. Pumps

**Date initiated:** Jan 2009 – FSCA for B.C. Infusion Pumps was initiated.

**Product issue:** Possible delay in therapy due to appearance of certain error codes.

**Company’s corrective action:** Upgrade of Pumps to higher configuration by Company

**Quantity affected:** approx 1700 pumps in Singapore

**Healthcare Institutions affected:**
4 major Healthcare Institutions
Case Study 2 – B.C. Pumps

Step 1
Health hazard evaluation

Step 2
Consultation with other stakeholders

Step 3
Communication of regulatory decision to company and finalise timelines.

Step 4
Communicate updates on FSCA to stakeholders (including other regulators)

Step 5
Review proposed device modification

Step 6
Monitor completion of FSCA and post-market performance

As device was manufactured in Singapore, information about this FSCA was communicated to the other regulatory agencies.
Case Study 3 – Branded Contact Lens

Chronology of events

1. Product recall for Branded contact lens initiated on 19 Aug 2010.

2. Over 900 boxes had been supplied at consumer level.

3. On 20 Aug 2010, teleconference was convened urgently to discuss product recall with Company representatives.

4. Recall strategy was fine-tuned and press release was finalised on 20 Aug 2010.

5. HSA press release and Company press release were issued jointly.

6. Product recall continues to be monitored.
Case Study 4 – B&L Contact Lens Solution

Infection-linked lens solution withdrawn globally

Bausch & Lomb product voluntarily taken off shelves for good 3 months after S’pore alert

BY SALMA KHALIK
Health Correspondent

EYECARE product maker Bausch & Lomb has taken its ReNu MoistureLoc contact lens solution off worldwide shop shelves for good — three months after Singapore sounded the alarm over its strong link to an outbreak of a fungal infection that can cause blindness.

The company’s move follows a stop to United States sales of ReNu MoistureLoc on April 13 after the Centers for Disease Control and Prevention (CDC) said it was investigating an unusual spike in infections among Americans using the product. At least eight victims there have needed corneal transplants.

Extensive federal checks of Bausch & Lomb’s factory in South Carolina, where ReNu MoistureLoc is made for the US and Asian markets, have turned up nothing, but the company said it was taking the “most responsible action” of discontinuing sales of the product, even where no “unusual trends” in infections had emerged.

For the Singapore eye surgeon who first raised the alert worldwide late last year and was met with disbelief from the US, it is vindication.

Associate Professor Donald Tan of the Singapore National Eye Centre, who first raised the alert over the contact lens solution’s strong link to an outbreak of a fungal infection that can cause blindness.
Investigation by HSA

Product development, quality systems
No non-conformities & compliance to GMP
Fusarium was NOT recovered from the factory, warehouse, solution infiltrate, unopened bottles

Local product testing
Passed sterility testing
Passed ISO 14729 test agst std & local isolates

Source of product
Counterfeiting ruled out

Genetic typing
US CDC report: multiple strains of fusarium solani (common point source not likely)

In-use efficacy??
Classic characteristic of a fungal keratitis – a stromal infiltrate with indistinct, feathery edges, and satellite lesions
Severe fungal keratitis, eventually requiring urgent therapeutic penetrating keratoplasty