CURRENT REGULATORY CHALLENGES RELATING TO HERBAL MEDICINES:
ADULTERATION OF HERBAL MEDICINES

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Outline of Presentation

- Current Regulatory Status In Malaysia
- Implementation of Hologram Meditag
- New Emerging Problem & Challenges
- Reactive & Proactive Approaches
- Impact & Outcome
- Adulteration in Traditional Herbal Medicines, Food and Food Supplement
- Conclusion
CURRENT REGULATORY STATUS
Situation in Malaysia

- Legislation
  A good set of laws & regulation in place including registration of medicinal products

- Regulatory
  WHO Collaborating Centre since 1996 / PICS member since 2002 as 26th member

- Enforcement
  Enforcement Officers (350 Officers) in 15 states

- Supply Chain – Poison / Control Items
  Govt. supply drugs to all its Health Institutions via controlled concession & contract co.- eg Pharmaniaga Sdn Bhd
  Private Sectors are licensed / inspected routinely for eg. Pharmacy premises & Pharmaceutical industries.

- Supply Chain – OTC / Traditional Medicine
  Wholesaler are licensed to sell
  Public Sectors and Private Sectors for retail are not licensed
  Facing challenges of adulterated herbal medicines and unregistered medicines/counterfeits
### Structure

<table>
<thead>
<tr>
<th>Regulatory Function</th>
<th>Responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensing of manufacturing</td>
<td>DCA/NPCB</td>
</tr>
<tr>
<td>Licensing of importation</td>
<td>DCA/NPCB</td>
</tr>
<tr>
<td>Licensing of wholesale trade</td>
<td>NPCB</td>
</tr>
<tr>
<td>GMP inspection</td>
<td>DCA/NPCB</td>
</tr>
<tr>
<td>Inspection of distribution channels</td>
<td>PSD</td>
</tr>
<tr>
<td>Product assessment &amp; registration</td>
<td>DCA/NPCB</td>
</tr>
<tr>
<td>Quality control</td>
<td>DCA/NPCB</td>
</tr>
<tr>
<td>Control of promotion &amp; information</td>
<td>PSD</td>
</tr>
<tr>
<td>ADR monitoring</td>
<td>DCA/NPCB</td>
</tr>
<tr>
<td>Price regulation</td>
<td>Free pricing</td>
</tr>
</tbody>
</table>

- **Control of Drugs & Cosmetics Regulations 1984**
  - Carried out by NPCB:
    - Product Evaluation
    - Product Analysis
    - GMP Inspection & Licensing
    - Post-Marketing Surveillance & ADR

[Diagram showing the structure of regulatory functions and responsible parties]
Legislation

The enabling powers that allow Ministry of Health Malaysia to control and regulate the wellness industry sector are embodied in the following legislations:

- Registration of Pharmacist Act 1951, revised 1989
- Poisons Act 1952 (revised 1989)
- Sale of Drugs Act 1952 (revised 1989)
- Control of Drugs and Cosmetics Regulations 1984
- Dangerous Drug Act 1952 (revised 1980)
- Medicines (Advertisement and Sale) Act (revised 1983)
Registration Status
1991 – October 2010

<table>
<thead>
<tr>
<th>Product category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Medicines (Prescriptions)</td>
<td>12,980</td>
</tr>
<tr>
<td>Non-prescriptions (OTC)</td>
<td>9,876</td>
</tr>
<tr>
<td>Natural Products (Traditional medicines)</td>
<td>20,668</td>
</tr>
<tr>
<td>Veterinary Products</td>
<td>45</td>
</tr>
<tr>
<td>Cosmetics (Notification)</td>
<td>236,735</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>280,304</strong></td>
</tr>
</tbody>
</table>

Effective 1st January 2008 Registration of Cosmetics replaced by Procedure of Notification
Implementation of Hologram Technology

One Hologram for all Medicinal Products to be marketed in Malaysia
- MeditagTM Hologram
  (1st in the world)


The latest edition (Sept 2006)
HOLOGRAM DECODER PLACE IN ALL PHARMACY PREMISES IN MALAYSIA

- Make available in the pharmacy premises
- Encourages the publics to check the products that they have bought for authenticity.
- Promotion and encourage publics to buy medicine in licensed premises (Pharmacy)
- Encourages the Pharmacist to check the product sold in their premises.
Challenges

- Unregistered products
- Adulteration in unregistered herbal products
- Adulteration in registered herbal products.
- Adulteration in food & Food Supplement
- Counterfeits products
- Smuggling, Illegal entry
- Parallel importation
- Diversion
- Tampering
- Repackaging & re-labeling
- Fake Hologram meditag™
Adulterants in Traditional products, Cosmetics, Food & Food Supplement

Steroids
  Dexamethasone, Betamethasone
Drugs for erectile dysfunction
  ED’s and their analogs
Antihistamines
  Chlorpheniramine
NSAI D’s
  Ibuprofen, Mefenamic acid, Indomethacin
Slimming Agents
  Sibutramine
  and their analogs
Antidiabetics
  Metformin, Glybenclamide

Source: NPCB, Malaysia
What is an analog?

The word **analog** or **analogue** is used to describe a substance that has a major chemical structures in common with another chemical.
# Sildenafil analogs

<table>
<thead>
<tr>
<th>Name</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sildenafil standard</td>
<td>C\textsubscript{22}H\textsubscript{30}N\textsubscript{6}O\textsubscript{4}S</td>
</tr>
<tr>
<td>Vardenafil standard</td>
<td>C\textsubscript{23}H\textsubscript{32}N\textsubscript{6}O\textsubscript{4}S</td>
</tr>
<tr>
<td>Tadalafil standard</td>
<td>C\textsubscript{22}H\textsubscript{19}N\textsubscript{3}O\textsubscript{4}</td>
</tr>
<tr>
<td>Homosildenafil</td>
<td>C\textsubscript{23}H\textsubscript{12}N\textsubscript{6}O\textsubscript{4}S</td>
</tr>
<tr>
<td>Hydroxyhomosildenafil</td>
<td>C\textsubscript{23}H\textsubscript{32}N\textsubscript{6}O\textsubscript{6}S</td>
</tr>
<tr>
<td>Acetildenafil</td>
<td>C\textsubscript{28}H\textsubscript{34}N\textsubscript{6}O\textsubscript{3}</td>
</tr>
<tr>
<td>Noracetildenafil</td>
<td>C\textsubscript{24}H\textsubscript{32}N\textsubscript{6}O\textsubscript{3}</td>
</tr>
<tr>
<td>Hydroxyacetildenafil</td>
<td>C\textsubscript{25}H\textsubscript{34}N\textsubscript{6}O\textsubscript{4}</td>
</tr>
<tr>
<td>Piperadino acetildenafil</td>
<td>C\textsubscript{24}H\textsubscript{31}N\textsubscript{6}O\textsubscript{3}</td>
</tr>
<tr>
<td>Piperadino vardenafil</td>
<td>C\textsubscript{22}H\textsubscript{29}N\textsubscript{5}O\textsubscript{4}S</td>
</tr>
<tr>
<td>Aminotadalafil</td>
<td>C\textsubscript{21}H\textsubscript{16}N\textsubscript{4}O\textsubscript{4}</td>
</tr>
<tr>
<td>Dimethyl sildenafil (aildenafil)</td>
<td>C\textsubscript{23}H\textsubscript{32}O\textsubscript{4}N\textsubscript{6}S</td>
</tr>
<tr>
<td>Sildenafil thione (sulfsildenafil)</td>
<td>C\textsubscript{22}H\textsubscript{30}O\textsubscript{3}N\textsubscript{6}S\textsubscript{2}</td>
</tr>
<tr>
<td>Sildenafil thione (sulfohomosildenafil)</td>
<td>C\textsubscript{23}H\textsubscript{32}O\textsubscript{3}N\textsubscript{6}S\textsubscript{2}</td>
</tr>
<tr>
<td>Dimethyl sildenafil thione (sulfoaildenafil)</td>
<td>C\textsubscript{23}H\textsubscript{32}O\textsubscript{3}N\textsubscript{6}S\textsubscript{2}</td>
</tr>
<tr>
<td>Benzamidenafil**</td>
<td>C\textsubscript{40}H\textsubscript{23}N\textsubscript{3}O\textsubscript{6}</td>
</tr>
</tbody>
</table>
Common combination of adulterants

FOUND IN TRADITIONAL MEDICINE SAMPLES

- Chlorpheniramine + Dexamethasone
- Hydroquinone + Tretinoin
- Dexamethasone + Ibuprofen + Chloramphenicol + Chlorpheniramine
- Chlorpheniramine + Dexamethasone + Betamethasone + Prednisolone

Source: NPCB, Malaysia
<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>1</td>
</tr>
<tr>
<td>2006</td>
<td>8</td>
</tr>
<tr>
<td>2007</td>
<td>8</td>
</tr>
<tr>
<td>2008</td>
<td>13</td>
</tr>
<tr>
<td>2009</td>
<td>8</td>
</tr>
<tr>
<td>2010 (Oct)</td>
<td>7</td>
</tr>
</tbody>
</table>

*Source: NPCB, Malaysia*
WHAT CAN WE DO?

REACTIVE & PROACTIVE APPROACHES
Intelligence sampling

- Malaysian Life Style demanding :-
  - Slimming Products
    - women
  - Sex Stimulant Products
    - men
  - Bleaching Agent in cosmetics

Signal to look for

Prices, labels, claims
Proactive Approach

- **Demand Reduction**
  Eg Public Awareness Campaign, Exhibition, Pamphlets, Press Release, Media Coverage during operation etc

- **National Task Force**
  Headed by Enforcement Division Ministry of Internal Trade include Royal M’sian Police, Royal M’sian Custom, Immigration Dept., Pharmacy Enforcement MOH etc

- **New Pharmacy Bill**
  Consolidate the 5 Act including Poison Act 1952, Sale of Drug Act 1952

- **Training for officers**
  Workshop, Courses, Briefing during Meetings, Seminars etc

- **Co-Operation with Industry / Product Owners**
  Discussion for Action When unregistered/Counterfeit Products Detected

- **Regional/Global Networking**
  Through Meetings/Seminar, Constant Contact eg e-mail (eg.PMAS)
Restoring the trust in Marketplace

- “Know Your Medicine” campaign
- posters/post-cards/Calendars with message
- Newspapers
- TV, radio and public talks
- School exhibitions
- Customers Day
- Road-shows on holograms
- Media announcements & Adv.
- Increase consumers awareness about the risk of adulterated products and unregistered products.
Emerging
Problem & Challenges
WAY FORWARD-
Strengthening Enforcement

• More branches
• Increase manpower - currently 352 posts
• Continuous education
• Human capital development priority
• Post-graduate studies
• Incentive & critical allowances
• Forensic Laboratory
• Vigilant at entry points
• R&D
• New Pharmacy Bill – addressing counterfeit medicine & Stiffer Penalty
Strengthening Enforcement

- New Pharmacy Bill – addresses:
  - Counterfeit medicines
  - Adulterated products and Herbal Products
  - Unregistered products
  - Expired products

- Penalties:
  - Minimum mandatory Jail sentence
  - Deterrent fines 10x the existing fine
WAY FORWARD - Collaboration - National

- Ministry of Domestic Trade & Consumer Affairs
- Customs Department
- Police
- Pharmaceutical Industry
- Consumer Association
- Health Professional Group
WAY FORWARD - International Networking

- WHO – IMPACT
- PIC/S – Rapid Alerts
- ACCSQ PPWG – Post Marketing Alert System
- ASEAN WGTCP
- Bilateral & Multi-lateral Cooperation
IMPACT & OUTCOME
Consumer Education & Dialogues
2005 – Oct 2010

<table>
<thead>
<tr>
<th>Year</th>
<th>Talks</th>
<th>Exhibitions</th>
<th>Dialogues</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>43</td>
<td>60</td>
<td>5</td>
</tr>
<tr>
<td>2007</td>
<td>80</td>
<td>155</td>
<td>11</td>
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<tr>
<td>2008</td>
<td>213</td>
<td>290</td>
<td>22</td>
</tr>
<tr>
<td>2009</td>
<td>220</td>
<td>309</td>
<td>44</td>
</tr>
<tr>
<td>2010</td>
<td>281</td>
<td>370</td>
<td>28</td>
</tr>
</tbody>
</table>
Research & Development:

- Study on Public Awareness and Behavior Towards The Control of Medication Sales and Usage in Malaysia. (The Multicenter Study was done in 2005 and 2007)

From the study – the result of public knowledge on registered medicine in Malaysia has increased from 59% (in 2005) to 70% (in 2007).
Since the introduction of meditag hologram in 2005, there has been a significant increase in the identification and confiscation of illegal items from the market and prevented their entry into distribution channels. As a result, consumer confidence in the integrity of pharmaceuticals has increased and public health has been safeguarded.
Emerging Trend - ADULTERATION IN FOOD SUPPLEMENT & BEVERAGES
Adulteration of Sildenafil in food- coffee mixture
Conclusion

- Adulterated Herbal Medicines & Counterfeits a global issue
  - Address the issue: the whole supply chain
  - Established size and scope of problem objectively
- Serious treat to public health and safety
- Combat through multi-pronged and holistic approach.
- Strong political will
- Sound legal framework - New & revised laws
- Reputable regulatory system – Registration, Licensing, Surveillance, Testing, ADR Monitoring, Information
- Established enforcement system – Inspection, Investigation, Prosecution, Confiscation, Consumer Education
- Strengthening collaboration – National & International, Inter and Intra Agencies, Consumer groups, Professional bodies, right owners
- Advanced Security technology – ICT, Security labels or embedded (hologram), bank note style security threads
- Public Awareness and education to reduce the demand for adulterated, unregistered and counterfeit products.
TERIMA KASIH
THANK YOU