REGULATORY CONTROL FOR HERBAL/TRADITIONAL MEDICINES AND HEALTH SUPPLEMENT PRODUCTS IN MALAYSIA

11th MARCH 2015
DATIN SHANTINI THEVENDRAN
COMPLEMENTARY SECTION, PPP, NPCB
CONTENTS

- Definition
- Product Registration Process
- Registration Criteria
- Safety, Quality, Efficacy / claimed benefits
- Statistics
**Voluntary registration of API commenced in April 2011. Registration of generic API will be announced at a later date.**
What is a Traditional Medicine?

- **Traditional medicine** is defined as any product used in the practice of indigenous medicine, in which the drug consists solely of one or more naturally occurring substances of a **plant**, **animal** or **mineral**, or parts thereof, in the **unextracted** or **crude extract** form.

- **Indigenous medicine** is defined as a system of treatment and prevention of disease established through traditional use of naturally occurring substances.
Active Ingredients:
- Toxic constituents/substances exceeding stipulated limits
- Narcotics
- Psycotropics

Others:
- Isolated and chemical characterized substances
- Extemporaneous preparations
- Vaccines
- Human parts derivatives
- Sterile preparations
- Product in food presentations (incl. beverages)
Traditional medicine claims

Traditionally used...

- Traditional general claims
  - general health
- Traditional medium claims
  - reduction of risk of a disease/disorder
  - relief of symptoms
  - aids/assists in the management of a named symptom/disease
  - prevents/stops/slow down the progress of a mild/self-limiting disease or medical condition
Finished herbal products:

herbal preparations made from one or more herbs. If more than one herb is used, the term mixture herbal product can also be used. Finished herbal products and mixture herbal products may contain excipients in addition to the active ingredients. However, finished products or mixture products to which chemically defined active substances have been added, including synthetic compounds and/or isolated constituents from herbal materials, are not considered to be herbal.

*World Health Organization (WHO) Guidelines (4th October 2010)*
Herbal product claims

General health maintenance
Medium claims
- reduction of risk of a disease/disorder
- relief of symptoms
- aids/assists in the management of a named symptom/disease
High claims
- treats/cures/manages any disease/disorder
- adjunct/to complement any treatment

GUIDELINES: final draft
IMPLEMENTATION: 2015
A Health Supplement (HS) means any product that is used to supplement a diet and to maintain, enhance and improve the health function of human body.

It is presented in small unit dosage forms (to be administered) such as capsules, tablets, powder, liquids and shall not include any sterile preparations (i.e. injectables, eye drops).

(Malaysian DRGD 2014 July)
Health supplements may contain one or more, or the following combination:

i) Vitamins, minerals, amino acids, fatty acids, enzymes, probiotics, and other bioactive substances;

ii) Substances derived from *natural sources, including animal, mineral and botanical materials in the forms of extracts, isolates, concentrates, metabolite;

iii) Synthetic sources of ingredients mentioned in (i) and (ii) may only be used where the safety of these has been proven.
Claims for Health Supplements

- General or Nutritional Claims
- Functional Claims
- Disease Risk Reduction Claims

Effective 1\textsuperscript{st} March 2013
Maximum Daily Levels of Vitamins and Minerals for Adults allowed in Health Supplements

<table>
<thead>
<tr>
<th>NO.</th>
<th>VITAMINS &amp; MINERALS</th>
<th>UPPER DAILY LIMIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Vitamin A</td>
<td>5000 IU</td>
</tr>
<tr>
<td>2.</td>
<td>Vitamin D</td>
<td>1000 IU</td>
</tr>
<tr>
<td>3.</td>
<td>Vitamin E</td>
<td>800 IU</td>
</tr>
<tr>
<td>4.</td>
<td>Vitamin K (K1 and K2)¹</td>
<td>0.12mg</td>
</tr>
<tr>
<td>5.</td>
<td>Vitamin B1 (Thiamine)</td>
<td>100 mg</td>
</tr>
<tr>
<td>6.</td>
<td>Vitamin B2 (Riboflavin)</td>
<td>40 mg</td>
</tr>
<tr>
<td>7.</td>
<td>Vitamin B5 (Pantothenic Acid)</td>
<td>200 mg</td>
</tr>
<tr>
<td>8.</td>
<td>Vitamin B6 (Pyridoxine)</td>
<td>100 mg</td>
</tr>
<tr>
<td>9.</td>
<td>Vitamin B12 (Cyanocobalamin)</td>
<td>0.6 mg</td>
</tr>
<tr>
<td>10.</td>
<td>Vitamin C (Ascorbic Acid)</td>
<td>1000 mg</td>
</tr>
<tr>
<td>11.</td>
<td>Folic Acid</td>
<td>0.9 mg</td>
</tr>
<tr>
<td>12.</td>
<td>Nicotinic Acid</td>
<td>15 mg</td>
</tr>
<tr>
<td>13.</td>
<td>Niacinamide (Nicotinamide)</td>
<td>450 mg</td>
</tr>
<tr>
<td>14.</td>
<td>Biotin</td>
<td>0.9 mg</td>
</tr>
<tr>
<td>15.</td>
<td>Boron</td>
<td>6.4 mg</td>
</tr>
<tr>
<td>16.</td>
<td>Calcium</td>
<td>1200 mg</td>
</tr>
<tr>
<td>17.</td>
<td>Chromium</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>18.</td>
<td>Copper</td>
<td>2 mg</td>
</tr>
<tr>
<td>19.</td>
<td>Iodine</td>
<td>0.3 mg</td>
</tr>
<tr>
<td>20.</td>
<td>Iron ²</td>
<td>20 mg</td>
</tr>
<tr>
<td>21.</td>
<td>Magnesium</td>
<td>350 mg</td>
</tr>
<tr>
<td>22.</td>
<td>Manganese</td>
<td>3.5 mg</td>
</tr>
<tr>
<td>23.</td>
<td>Molybdenum</td>
<td>0.36 mg</td>
</tr>
<tr>
<td>24.</td>
<td>Phosphorus</td>
<td>800 mg</td>
</tr>
<tr>
<td>25.</td>
<td>Selenium</td>
<td>0.2 mg</td>
</tr>
<tr>
<td>26.</td>
<td>Zinc</td>
<td>15 mg</td>
</tr>
</tbody>
</table>

Vitamins/ Minerals:
- Daily levels must not exceed maximum daily levels for adults allowed in health supplement.
- For pre and antenatal use, as part of a multivitamin and mineral preparation, levels higher than the 20mg limit established for adults may be permitted at the discretion of the Authority.

Ref: ASEAN Guidelines for HS
SUMMARY OF CLAIMS

Complementary medicine

TM
  General
  Medium

Herbal
  Medium
  High

HS
  General
  Functional claim
  Disease risk reduction
Sources of evidence – TM/Herbal

- **Scientifically established treatment claims**
  - Human intervention study

- **Medium claims**
  - Controlled trials / analytical studies / epidemiological cohort / case-control studies
  - Evidence from multiple time series
  - TM formulary

- **General claims**
  - TM Pharmacopoeia/monographs
  - Documented history of use
  - Reference organizations
Sources of evidence - HS

- Disease risk reduction: Human intervention study
- Functional claims: Human observational studies, Animal studies
- General claims: Authoritative reference texts, International organizations or recognized regulatory authorities
ON-LINE REGISTRATION

National Pharmaceutical Control Bureau
http://www.bpfk.gov.my – Quest 3
1) National Pharmaceutical Control Bureau:
http://www.bpfk.gov.my – Regulatory Information

2) Drug Registration Guidance Document

PREAMBLE

This “DRUG REGISTRATION GUIDANCE DOCUMENT” will serve as the reference guide for both pharmaceutical products for human use and traditional products. It will replace the “Guidelines for Application for Registration of Pharmaceutical Products” Third Edition of October 1996 and “Garis Panduan Permohonan Pendaftaran Kebangsaan Ubat Tradisional” Second Edition, December 1998. The contents of this version include:

- Updated information relating to administrative requirements and procedures.
- Information on Drug Control Authority (DCA) policies currently applicable.
- Guidelines on the on-line application process and requirements which will incorporate the ASEAN technical requirements and standards for pharmaceuticals (where applicable).

An on-going review of policy matters will continue, taking into account the global regulatory environment, to allow for timely and pertinent changes.

Information relating to DCA policy decisions is current up to its 220th meeting on 01 October 2009. Please visit the National Pharmaceutical Control Bureau (NPCB) website at http://www.bpfk.gov.my for updates in regulatory information.

March 2010 Revision
Product Registration Application
QUEST 3 LAYOUT
Screening by Head of Unit

Registration Fee Payment

Further evaluation by Assessor

Meeting of Products Evaluation Committee (within NPCB)

Meeting of Drug Control Authority

Issue registration number (MALxxxxxxxxxxN/T)

Product registration holder (PRH)

PRH

Send letter of rejection to PRH

Approve

Reject

Incomplete

Complete

Incomplete

Reply Through Quest 3 to comply to our requirements
Product Registration Number

MAL2014.... “Code”

A: Scheduled Poisons
X: Non-scheduled Poisons
   (over the counter products)
T: Traditional Medicines
N: Health Supplements
C: Contract Manufacturer
E: Export Only
R: Repacked
S: Second source

- Validity period of registration – 5 years
- Renewal of product registration should be done not later than 6 month prior to expiry of product registration
### CLIENT’S CHARTER

<table>
<thead>
<tr>
<th>Category</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCE &amp; Biotech</td>
<td>&lt; 245 working days</td>
</tr>
<tr>
<td>Generics &amp; OTC</td>
<td>&lt; 210 working days</td>
</tr>
<tr>
<td>TM &amp; HS (high claims)</td>
<td>&lt; 210-245 working days</td>
</tr>
<tr>
<td>TM &amp; HS (single ing)</td>
<td>&lt; 113 working days</td>
</tr>
<tr>
<td>TM &amp; HS (comb)</td>
<td>&lt; 136 working days</td>
</tr>
</tbody>
</table>

On condition: Full Compliance to Requirements
FEES

• PROCESSING FEES
  - Pharmaceuticals  RM 1000
  - Traditional      RM 500
  - Cosmetics        RM 50

• LABORATORY TESTING
  - Pharmaceuticals  RM 1200-2000
  - Traditional     RM 700
REGULATORY REQUIREMENTS

Quality
Status of manufacturer

Safety
maximum daily limits
Heavy metals
Microorganisms

Efficacy
As claimed
<table>
<thead>
<tr>
<th>Fields</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Name of Product</td>
</tr>
<tr>
<td>A2</td>
<td>Product Description</td>
</tr>
<tr>
<td>A3</td>
<td>Dosage Form</td>
</tr>
<tr>
<td>A4</td>
<td>Name and Strength of Active and Excipient Substance</td>
</tr>
<tr>
<td>A5</td>
<td>Product Indication</td>
</tr>
<tr>
<td>A6</td>
<td>Dose / Usage instruction</td>
</tr>
<tr>
<td>A7</td>
<td>Contraindication</td>
</tr>
<tr>
<td>A8</td>
<td>Warning / Precaution</td>
</tr>
<tr>
<td>A9</td>
<td>Drug Interaction</td>
</tr>
<tr>
<td>A10</td>
<td>Side Effects / Adverse Reaction</td>
</tr>
<tr>
<td>A11</td>
<td>Signs of Overdose</td>
</tr>
<tr>
<td>A12</td>
<td>Storage Condition</td>
</tr>
<tr>
<td>A13</td>
<td>Shelf Life</td>
</tr>
<tr>
<td>A14</td>
<td>Therapeutic Code</td>
</tr>
</tbody>
</table>
# SECTION B
## PRODUCT FORMULA

<table>
<thead>
<tr>
<th>Fields</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>B 1.1</td>
<td>Batch Manufacturing Formula</td>
</tr>
<tr>
<td>B 1.2</td>
<td>Attachment of Batch Manufacturing</td>
</tr>
<tr>
<td>B 2.1</td>
<td>Manufacturing process</td>
</tr>
<tr>
<td>B 2.2</td>
<td>Attachment of manufacturing</td>
</tr>
<tr>
<td>B 3.0</td>
<td>In Process Quality Control</td>
</tr>
</tbody>
</table>
## SECTION C
PACKING

<table>
<thead>
<tr>
<th>Fields</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Pack Size</td>
</tr>
</tbody>
</table>
| C2     | Container Type /Container Type Description  
         e.g. : HDPE Plastic Bottle, Glass Bottle, Aluminum Blister Pack |
| C3     | Barcode/Serial Number |
| C4     | Recommended Distributor’s Price, RM |
| C5     | Recommended Retail Price, RM |
SECTION D
LABELS & PACKAGE INSERT

<table>
<thead>
<tr>
<th>Fields</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D 1</td>
<td>Label (mock up) for immediate container</td>
</tr>
<tr>
<td>D 2</td>
<td>Label (mock up) for outer carton</td>
</tr>
<tr>
<td>D 3</td>
<td>Proposed package insert</td>
</tr>
</tbody>
</table>
SECTION E
PARTICULARS OF THE MANUFACTURER/ IMPORTER / REPACKER/ PRODUCT OWNER/STORE ADDRESS

<table>
<thead>
<tr>
<th>Fields</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E 1</td>
<td>Product Owner</td>
</tr>
<tr>
<td>E 2</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>E 3</td>
<td>Repacker</td>
</tr>
<tr>
<td>E 4</td>
<td>Other Manufacturer(s) Involved ( If Any)</td>
</tr>
<tr>
<td>E 5</td>
<td>Store Address</td>
</tr>
<tr>
<td>E 6</td>
<td>Importer</td>
</tr>
<tr>
<td>Fields</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>F 1.0</td>
<td>Letter of Authorisation from Product Owner</td>
</tr>
<tr>
<td>F 2.1</td>
<td>Letter of Appointment of Contract manufacturer from Product Owner</td>
</tr>
<tr>
<td>F 2.2</td>
<td>Letter of Acceptance from Contract Manufacturer</td>
</tr>
<tr>
<td>F 3.0</td>
<td>Is the Active Substance(s) Patented in Malaysia</td>
</tr>
<tr>
<td>F 4.0</td>
<td>Certificate of Pharmaceutical Product (CPP)</td>
</tr>
<tr>
<td>F 5.0</td>
<td>Certificate of Free Sale (CFS)</td>
</tr>
<tr>
<td>F 6.0</td>
<td>Good Manufacturing Practice (GMP) Certificate</td>
</tr>
<tr>
<td>F 7.0</td>
<td>Summary of Product Characteristics (Product Data Sheet – if any)</td>
</tr>
<tr>
<td>F 8.0</td>
<td>Patient Information Leaflet (PIL)</td>
</tr>
<tr>
<td>F 9.0</td>
<td>Attachment of Protocol Analysis</td>
</tr>
<tr>
<td>F 10</td>
<td>Attachment of Certificate Analysis (Finished Product)</td>
</tr>
<tr>
<td>F 11</td>
<td>Attachment of Certificate of Analysis (Active Ingredient)</td>
</tr>
<tr>
<td>F 12</td>
<td>Other Supporting Document</td>
</tr>
</tbody>
</table>
SAFETY CRITERIA

- Limits for heavy metals
- Limits for microbial contamination
- Absence of steroids and other adulterants
- Indications and claims
- Prohibition of herbs/ingredients with known adverse effects
- Labeling
SCREENING FOR ADULTERANTS

Based on product indications:

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men’s health</td>
<td>e.g. Sildenafil, Tadalafil and its analogues</td>
</tr>
<tr>
<td>Slimming</td>
<td>e.g. Fenfluramine</td>
</tr>
<tr>
<td>Muscle and joint pains</td>
<td>e.g. NSAIDs, Steroids</td>
</tr>
<tr>
<td>Cough and cold</td>
<td>e.g. Anti- histamines</td>
</tr>
</tbody>
</table>
For products containing Red Yeast Rice (*Monascus purpureus*), applicants shall provide certificates of analysis (for both raw material and finished product) showing the Monacolin-K content.

The percentage of Monacolin-K shall not exceed 1% and the Monakolin-K consumed shall not exceed 10 mg per day.
Supporting Documents for New Active Ingredients/ New Dose

Reference Countries
- United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan and Switzerland
- Must be provided from competent authorities (e.g. US FDA, TGA, Health Canada)
- Examples: Registration status, established monograph

Clinical Studies / Scientific Evidences / Researches
- Full articles from the published journals
- Examples: Human clinical studies, scientific reviews, animal toxicological studies etc

Established References
- Examples: Martindale, Pharmacopeias, US PDR, The Merck Index etc
QUALITY CRITERIA

HEAVY METAL SPECIFICATION

Mercury - not more than 0.5 ppm
Arsenic - not more than 5.0 ppm
Lead  - not more than 10 ppm
Cadmium - not more than 0.3 ppm
QUALITY CRITERIA

12.6 QUALITY CONTROL TEST SPECIFICATIONS FOR TRADITIONAL MEDICINE PRODUCTS

1. **Limit Test for Heavy Metals**
   
   Maximum limit for heavy metals:
   
   1.1 Lead : NMT 10.0 mg/kg or 10.0 mg/litre (10.0ppm)
   1.2 Arsenic : NMT 5.0 mg/kg or 5.0 mg/litre (5.0ppm)
   1.3 Mercury : NMT 0.5 mg/kg or 0.5 mg/litre (0.5ppm)
   1.4 Cadmium : NMT 0.3 mg/kg or 0.3 mg/litre (0.3ppm)

2. **Disintegration Test (for tablets, capsules and pills)**
   
   Disintegration time
   
   2.1 Uncoated tablets : NMT 30 minutes
   2.2 Film-coated tablets : NMT 30 minutes
   2.3 Sugar-coated tablets : NMT 60 minutes
   2.4 Enteric-coated tablets : Does not disintegrate for 120 minutes in acid solution but to disintegrate within 60 minutes in buffer solution
   2.5 Capsules : NMT 30 minutes
   2.6 Pills : NMT 120 minutes

3. **Test for Uniformity of Weight (tablets and capsules only)**
   
   Not more than 2 capsules / tablets exceed the limit by ± 10% from the average weight AND no tablet / capsule exceed the limit by ± 20% from the average weight.

4. **Test for Microbial Contamination**

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>TAMC (CFU/g or CFU/ml)</th>
<th>TYMC (CFU/g or CFU/ml)</th>
<th>Test for Specified Microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10²</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>Oromucosal Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10¹</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>Gingival Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10¹</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>Cutaneous Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10¹</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>Nasal Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10¹</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>Auricular Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10¹</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>Vaginal Use</td>
<td>NMT 2 x 10²</td>
<td>NMT 2 x 10¹</td>
<td>- Absence of Staphylococcus aureus in 1g or 1ml</td>
</tr>
<tr>
<td>SAFETY</td>
<td>QUALITY</td>
<td>INDICATIONS &amp; CLAIMS</td>
<td>LABELLING</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>• Absence of banned/prohibited ingredients</td>
<td>• Compliance with Good Manufacturing Practices</td>
<td>• Low level claims supported by documents/literature on traditional use</td>
<td>• Full ingredient listing</td>
</tr>
<tr>
<td>• Pre registration testing</td>
<td>• Limits for disintegration time</td>
<td>• Prohibition on claims for 20 diseases as stipulated in the Medicines (Advertisement &amp; Sale) Act</td>
<td>• Name of Marketing Authorization Holder</td>
</tr>
<tr>
<td>• Heavy metals – Mercury, Arsenic, Lead, Cadmium</td>
<td>• Uniformity of weight</td>
<td>• Revocation of license if found to be making false / unauthorized claims</td>
<td>• Name of manufacturer (and repacker, if any)</td>
</tr>
<tr>
<td>• Microbial limit test</td>
<td>• Stability data</td>
<td></td>
<td>• Serialized Security label (Hologram )</td>
</tr>
<tr>
<td>• Adulterants</td>
<td>• Evidence of marketing authorization in exporting country</td>
<td></td>
<td>• Warning statements</td>
</tr>
<tr>
<td>• Prohibition on the use of premixes</td>
<td></td>
<td></td>
<td>• Precautions</td>
</tr>
<tr>
<td>• Declaration that product is free from TSE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ADR reporting</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Label

- Name and Strength of active substances
- RDA (optional)
- Preservative(s) (where present)
- Alcohol (where present)
- Indication
- Dose / Use Instruction
- Functional Claim (if applicable)
- Warnings (if applicable)
- Storage Condition
- Keep out of reach of children / Jauhi dari kanak-kanak
- Pack Size
- Dosage Form
- Name & address of Product Registration Holder
- Name & address of Manufacturer
- Sources (animal origin)
- Source of capsule shell (if applicable)
- Batch Number
- Manufacturing Date
- Expiry Date

MAL ............................................
**HOLOGRAM MEDITAG®**

SECURITY FEATURES

- Both overt (visible) and covert (hidden)
Challenges

- TM and HS have differences in their functions, requiring different ‘tools’ for the pre market control and assessment for the risks.
- TM can not only be seen as a trade commodity but also as a comprehensive health care involving traditional practitioner.
- Doses and usage of the same ingredients may be different.
- Selective publication of study results (limited research budget).
- CAM products in most countries are not required to be registered.
- Ingredient or product?
Challenges

- New active ingredients
- Products of new combinations of active ingredients
- New claims
- New technology (e.g. bilayer technology)
- New invention (e.g. new dosage form, extended release/slow release)
Challenges

- Adulteration
- Illegal Manufacturing
- Unregistered Products
- Slick marketing campaigns involving unsubstantiated gimmicky products
- Misleading Claims
- Premix
THE WAY FORWARD

- Educating the public about current CAM evidence
- More quality research
- Intellectual property protection
- CAM to be used as adjunct to modern medicine (complementary)
- CAM to be used in place of conventional therapy (alternative)
- Physicians being oriented to CAM modalities and philosophy
THE WAY FORWARD

- Official analytical methods
- Pre-cleared information - Recognized standards monographs
- Herbal reference standards
- Competent expertise
- Laboratories
The Malaysian Herbal Monographs Vol. 1, 2 & 3.
On-going research projects

- Gamma Aminobutyric Acid (GABA) active ingredient
  - GABA will be prohibited until data of it’s safety and recommended dosage can be provided.

- Active ingredients containing naturally occurring Theophylline and Caffeine.
  - Assessment of the level of Theophylline and Caffeine in registered products will be done starting with the list of registered products in QUEST 2.
  - Maximum level of Theophylline/ Caffeine will be set based on safety assessment for traditional products
Quantification of α & β-asarone in finished traditional products
-α and β-asarone were reported to cause toxicity and carcinogenicity in mammals
- EMEA has set the safety level as not more than 115 µg/ day or 2 µg/ kg bw/ day
- On-going assessment of the levels of α and β-asarone on registered finished products on the market
- To conduct a pilot study starting with the CHINESE PHILOSOPHY OF USE first, followed by the other traditional practices later

- A working group will be formed to address the issues and prepare a guideline for the convenience of the industry

- The committee may wish to list our the acceptable references
## NEW INDICATIONS FOR Traditionally used ..........

### BASED ON PHILOSOPHY OF USE – EXAMPLES

<table>
<thead>
<tr>
<th>PRODUCT NAME</th>
<th>INDICATION REGISTERED</th>
<th>INDICATION BASED ON THE PHILOSOPHY</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC Tablet</td>
<td>Traditionally used for general health</td>
<td>Deficient and insecure exterior pattern manifested as spontaneous sweating, aversion to wind, bright pale complexion or people with weak constitution who are susceptible to wind</td>
</tr>
<tr>
<td>Dang Gui Bu Wie Tang Extract XYZ</td>
<td>Traditionally used for improving blood circulation</td>
<td>To tonify Qi and nourish blood</td>
</tr>
<tr>
<td>DEF</td>
<td>Traditionally used for reducing toothache</td>
<td>Stomach heat with yin deficiency, marked by fever, thirst, headache, toothache, nosebleed, hemoptysis, red tongue with white or dry yellow coating and rapid pulse</td>
</tr>
</tbody>
</table>
**REPORT ON SUSPECTED ADVERSE DRUG REACTIONS**

**NATIONAL CENTRE FOR ADVERSE DRUG REACTIONS MONITORING**

(www.madac.gov.my/madac)

(Please report all suspected drug reactions, including those for vaccines and traditional medicines. Do not hesitate to report if some details are not known. Identities of Reporter, Patient and Institution will remain Confidential.)

**REPORT No: [illegible]**

**A. PATIENT INFORMATION**

<table>
<thead>
<tr>
<th>Initials or R/N only</th>
<th>Age</th>
<th>Sex</th>
<th>Wt(kg)</th>
<th>Ethnic Group</th>
<th>Hospital/Clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li2949</td>
<td>73</td>
<td>Male</td>
<td></td>
<td>Javan</td>
<td></td>
</tr>
</tbody>
</table>

**B. ADVERSE REACTION DESCRIPTION**

- **Passage of black stool over 1 week**
  - Episodes: 6
  - Four episodes of gastrointestinal bleeding, acute renal failure, and hematuria

**Time to onset of reaction (hour/day):** 1 month
**Date of reaction:** 18.9.2007
**Reaction subsided after stopping drug / reducing dose:** Yes
**Reaction reappeared after reintroducing drug:** No

**Treatment of adverse reaction:** Surgical relief and IV corticosteroids
**Outcome:** Recovered

**Suspected drugs & other drugs used**

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Reg. No. &amp; Batch No.</th>
<th>Therapy Dates</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional Medicine</td>
<td>[illegible]</td>
<td>Joint pain</td>
<td>Increase strength of the body</td>
</tr>
</tbody>
</table>

**D. RELEVANT INVESTIGATIONS/ LABORATORY DATA**

**E. RELEVANT HISTORY (e.g. hepatic/renal dysfunction, allergies, etc.)**

**F. REPORTER**

<table>
<thead>
<tr>
<th>Name</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>[illegible]</td>
<td>[illegible]</td>
<td>18.9.2007</td>
</tr>
</tbody>
</table>

**Suspected Drug:** Traditional Medicine
Local Report: Whitening Cream

- Information on product used and where it was purchased was provided
- Sample taken for testing and was found to contain 25% hydroquinone
- Actions taken:
  - GMP audit done of manufacturing premise
  - Found gross violation of GMP principles
  - Manufacturer instructed to shut down
  - Total product recall
  - Decision made not to allow use of hydroquinone in Over-The-Counter products
Number of applications (payment made) (2010-2014)
TAMAN HERBA