Newsletter of the Drug Control Authority, Malaysia

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EVENTS

23RD ASEAN CONSULTATIVE COMMITTEE FOR STANDARDS AND QUALITY (ACCSQ) TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS PRODUCT WORKING GROUP (TMHS PWG) MEETING

This year, Malaysia proudly hosted the 23rd ASEAN Consultative Committee for Standards and Quality (ACCSQ) Traditional Medicines and Health Supplements Product Working Group (TMHS PWG) Meeting at the Berjaya Times Square Hotel, Kuala Lumpur. Held on 1 - 5 June 2015, the meeting is a harmonisation initiative for the regulation of Traditional Medicines and Health Supplement products in the ASEAN region.

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The objective of this meeting is to develop harmonisation schemes for Traditional Medicines and Health Supplement Products' regulations of ASEAN member countries to complement and facilitate the objective of the ASEAN Free Trade Area (AFTA), particularly, the elimination of technical barriers to trade posed by these regulations, without compromising on drug quality, safety and efficacy.

In addition to this meeting, discussions and technical pre-meetings were also held as below:

I. ASEAN TMHS Scientific Committee (ATSC)
II. Task Force on ASEAN Regulatory Framework
III. Task Force on ASEAN GMP

This successful event received overwhelming participation from 10 ASEAN countries, comprising of 138 participants including official delegates and observers from government agencies and the industry. Official representatives of ASEAN countries comprised of officers from the respective National Drug Regulatory Authority (NDRA).

NATIONAL REGULATORY CONFERENCE 2015 (NRC 2015)

The National Pharmaceutical Control Bureau (NPCB), Ministry of Health Malaysia successfully organised the National Regulatory Conference 2015 (NRC 2015). Officiated by Y.B. Datuk Seri Dr. S. Subramaniam, the Minister of Health Malaysia, this event was held at One World Hotel, Petaling Jaya, Selangor on the 4 - 6 August 2015.

The event received overwhelming participation from a total of 534 participants and speakers from within Malaysia and other countries. This includes a total of 34 foreign participants from Singapore, Indonesia, Hong Kong, Japan, Brunei Darussalam, Thailand, United States and Korea.

With the theme "Transformation Towards a New Regulatory Paradigm", the NRC 2015 aimed to deliver the latest regulatory information to the industry, academia, the regulatory agency of ASEAN countries as well as researchers from within Malaysia and abroad.

With both local and international speakers, the conference included a total of 10 plenary sessions on the 1st and 3rd day of the event. Whilst on the 2nd day, the conference was divided into 2 tracks i.e. Traditional Medicines and Health Supplements (TMHS), as well as Pharmaceutical and Biologic Products.

This conference serves as an important platform to increase awareness and understanding of the latest regulatory requirements for drugs in the country as well as to disseminate information related to the way forward of the Malaysian regulatory system. This in turn will contribute to the development of the pharmaceutical and health products industry in the country. In addition, the conference was also held to further strengthen cooperation between the participants of the conference which consisted of various relevant stakeholders.

VISIT BY THE SECRETARY GENERAL, MINISTRY OF HEALTH MALAYSIA

On 19 August 2015, YBhg. Datuk Dr. Chen Chaw Min, the Secretary General, Ministry of Health Malaysia, made his first official visit to the Pharmaceutical Services Division (PSD) and the National Pharmaceutical Control Bureau (NPCB) to gain first-hand information related to the Pharmacy Programme.

An official welcoming ceremony was held for the Secretary General where he was welcomed by the Senior Director of Pharmaceutical Services, YBhg. Dato' Eisah A. Rahman. A briefing, which included an introduction to the organisation, functions, activities, achievements and the future direction of the pharmacy programme was given by YBhg. Dato' Eisah A. Rahman. This occasion also saw the sharing of information related to other arising matters as well as the challenges that the Pharmacy Programme faces, including those related to NPCB.

Subsequently, the Secretary General then delivered a speech and addressed some of the issues raised during the briefing. This was followed by a short tour where he was also accompanied by Mr. Tan Ann Ling, the Director of Regulatory Pharmacy, NPCB to the Centre for Quality Control, NPCB as well as the Pharmacy Enforcement Forensics Laboratories at NPCB.

NEW DIRECTIVES

The following directives have been issued under Regulation 29 (1) of the Control of Drugs and Cosmetics Regulations 1984 by the Senior Director of Pharmaceutical Services, YBhg. Dato' Eisah A. Rahman.

1. ***Directive 4/15 [Ruj: (28) dlm. BPFK/PPP/07/25]: Restriction on Use of all Domperidone Products Due to Cardiovascular Adverse Effects***

Following the decision made by the Drug Control Authority (DCA) in its 287th Meeting on 30 April 2015, this directive is **to restrict the use of all domperidone products due to cardiovascular adverse effects.**

Therefore, the following instructions must be adhered to for **all domperidone products:**

THERAPEUTIC INDICATIONS
Domperidone is indicated for the relief of the symptoms of nausea and vomiting.

This includes:
- Nausea and vomiting of functional, organic, infectious or dietary origin.
- Nausea and vomiting induced by:
  - radiotherapy or drug therapy.
  - dopamine agonist (such as L-dopa and bromocriptine) used in the treatment of Parkinson's disease.

DOSAGE AND ADMINISTRATION
It is recommended to take [product name] 15 - 30 minutes before meals. If taken after meals, absorption of the drug is somewhat delayed.

Adults and adolescents ≥ 12 years and weighing ≥ 35kg and children weighing ≥ 35kg

The dose of [product name] should be the lowest effective dose for the individual situation (typically 30mg/day) and can be increased if necessary to a maximum daily oral dose of 40mg.

Usually, the maximum treatment duration should not exceed one week for the treatment of acute nausea and vomiting. If nausea and vomiting persists for longer than one week, patients should consult their physician. For other indications, the initial duration of treatment is up to four weeks. If treatment exceeds four weeks, patients should be re-evaluated and the need for continued treatment reassessed.

Formulation (domperidone per unit)	Dosage	Maximum dose per day
Film-coated tablets (10mg/tablet)	1 tablet three to four times per day	40mg (4x10mg tablet)
Oral suspension (1mg/mL)	10mL three to four times per day	40mg (40mL of 1mg/mL oral suspension)

Neonates, Infants and children <12 years of age and weighing <35kg, and adults and adolescents weighing <35kg

The dose of [product name] should be the lowest effective dose. The total daily dose is dependent on weight (see table below). Since metabolic functions and the blood-brain barrier are not fully developed in the first months of life, the risk of neurological side effects is higher in young children. Overdosing may cause nervous system disorders in children. The dose should be determined accurately based on body weight and not exceed the recommended maximum individual and daily dose in neonates, infants, toddlers and children.

Usually, the maximum treatment duration should not exceed one week for the treatment of acute nausea and vomiting. For other indications, the initial duration of treatment is up to four weeks. If treatment exceeds four weeks, patients should be re-evaluated and the need for continued treatment reassessed. Film-coated tablets and orodispersible tablets are unsuitable for use in children, adults and adolescents weighing less than 35kg. Suppositories are unsuitable for use in children.

Formulation (domperidone per unit)	Dosage	Maximum dose per day
Oral suspension (1mg/mL)	0.25mg/kg three to four times per day	1mg/kg but no more than 35mL (35mg)

Renal Impairment

Since the elimination half-life of domperidone is prolonged in severe renal impairment (serum creatinine > 6mg/100mL, i.e. >0.6mmol/L), the dosing frequency of [product name] should be reduced to once or twice daily, depending on the severity of the impairment, and the dose may need to be reduced. Patients with severe renal impairment should be reviewed regularly.

Hepatic Impairment

[Product name] is contraindicated for patients with moderate (Child-Pugh 7 to 9) or severe (Child-Pugh >9) hepatic impairment. Dose adjustment is not required for patients with mild (Child-Pugh 5 to 6) hepatic impairment.

CONTRAINDICATIONS

[Product name] is contraindicated in the following situations:

- Known hypersensitivity to domperidone or any of the excipients.
- Prolactin-releasing pituitary tumour (prolactinoma).
- In patients who have known existing prolongation of cardiac conduction intervals, particularly QTc, patients with significant electrolyte disturbances or underlying cardiac diseases such as congestive heart failure (see Warnings and Precautions).
- Co-administering with QT prolonging drugs.
- Co-administering with potent CYP3A4 inhibitors (regardless of their QT-prolonging effects).
- Whenever stimulation of gastric motility might be dangerous, e.g. in the presence of gastro-intestinal haemorrhage, mechanical obstruction or perforation.
- In patients with moderate or severe hepatic impairment.

WARNINGS AND PRECAUTIONS

Cardiovascular effects

Domperidone has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been very rare cases of QT-prolongation and torsades de pointes in patients taking domperidone. These reports included patients with confounding risk factors, electrolyte abnormalities and concomitant treatment which may have been contributing factors (see Adverse Reactions).

Epidemiological studies showed that domperidone was associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death (see Adverse Reactions). A higher risk was observed in patients older than 60 years, patients taking daily doses greater than 30mg, and patients concurrently taking QT-prolonging drugs or CYP3A4 inhibitors.

Domperidone should be used at the lowest effective dose in adults and children.

Domperidone is contraindicated in patients with known existing prolongation of cardiac conduction intervals, particularly QTc, in patients with significant electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia), or bradycardia, or in patients with underlying cardiac diseases such as congestive heart failure due to increased risk of ventricular arrhythmia (see Contraindications).

Electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia) or bradycardia are known to be conditions increasing the proarrythmic risk.

Treatment with domperidone should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patients should consult their physician.

Patients should be advised to promptly report any cardiac symptoms.

ADVERSE REACTIONS
{information to be included}

Postmarketing:
Cardiac Disorders
Frequency: Very rare
Ventricular arrhythmias, QTc prolongation, Torsade de Pointes, Sudden cardiac death (see Warnings and Precautions)

The package insert update process must be done according to these dates:
New registration and products under evaluation: **15 June 2015**
Registered products: **15 December 2015**

The application for amendments of package inserts must be done through variation application.

This directive is effective from **15 June 2015.**

2. ***Directive 5/15 [Ruj: (29) dlm. BPFK/PPP/07/25] Amendments to label, package inserts and Consumer Medication Information Leaflet (RiMUP) pertaining serious adverse effects to skin for products containing Paracetamol, including combination products.***

Following the decision made by the Drug Control Authority (DCA) in its 287th Meeting on 30 April 2015, this directive was issued ***for products containing Paracetamol, including combination products to amend label, package inserts and Consumer Medication Information Leaflet (RiMUP) pertaining serious adverse effects to skin.***

Therefore, the following instructions must be adhered to for **all products containing Paracetamol, whether single or as combination:**

The following statement must be stated on the label, package inserts and RiMUP (where related) for ALL products containing paracetamol:

Warning:

Allergy Alert: Paracetamol may cause severe skin reactions. Symptoms may include skin reddening, blisters or rash.
These could be signs of a serious condition. If these reactions occur, stop use and seek medical assistance immediately.

The following statement must be added to the Adverse Effect / Undesirable Effect section for products with package inserts:

Cutaneous hypersensitivity reactions including skin rashes, angioedema, Stevens Johnson Syndrome/ Toxic Epidermal Necrolysis have been reported.

The package insert update process must be done according to these dates:
New registration and products under evaluation: **15 June 2015**
Registered products: **15 December 2015**

The application for amendments of package inserts must be done through variation application.

This directive is effective from **15 June 2015.**

SUMMARY OF PRESS RELEASE

PUBLIC ANNOUNCEMENT REGARDING FORGED DOCUMENT FOR THE PRODUCT DOUBLE STEMCELL

The Ministry of Health Malaysia hereby attest that the document (letter) dated 14 May 2015 with the fake letterhead that reads DCA Established under the Control of Drugs and Cosmetics Regulations 1984 is a **forged document** and denies that it was issued by the DCA. The letter, in its contents, called for the sale of the product Double Stemcell owned by Phyto Science Sdn. Bhd. to be stopped for allegedly containing carcinogenic effect and thus being unsafe for human consumption.

Search of the NPCB database showed that an application for product classification was submitted for the product Phytoscience Double Stemcell (Powder) by the company Phyto Science Sdn. Bhd., whereby the product was classified as 'should be registered with the DCA under the `Health Supplement category'. To date, there is no product with the name Phytoscience Double Stemcell (Powder) by the company Phyto Science Sdn. Bhd. registered with the DCA.

All parties are reminded that forgery/falsification of documents is a criminal offense and if found guilty, offenders are punishable by law. Product sellers and distributors are also reminded that manufacture, sale, supply, importation, possession and administration of unregistered products is an offense under the Control of Drugs and Cosmetics Regulations 1984.

THE LETTER VERIFIED AS FORGED DOCUMENT

DRUG CONTROL AUTHORITY
Established under the Control of Drugs and Cosmetics Regulations 1984

Advisory: *2015-00526/P*

Dated: 14th May 2015

Attn:
Dato' Sri Lai Teck Peng (Chairman & CEO)
PHYTO SCIENCE SDN BHD (1013730P) (AJL932039)
Lot 56935, Jalan 9/8, Seksyen 9, 43650 Bandar Baru Bangi,
Selangor Darul Ehsan
Line: 603-89231880
Fax: 603-89231887 / 603-89231885
Website: www.iphytoscience.com

SUBJECT: IMMEDIATELY CEASE UNNOTIFIED PRODUCT DOUBLE STEMCELL™ POSSESS CARCINOGENIC EFFECTS & FOUND NOT TO BE FIT FOR HUMAN CONSUMPTION

The Drug Control Authority (DCA) has received unnotified Food supplement product Double Stemcell™ from a non-governmental organization. The product was tested by Central Laboratory using the allowable parameters set by DCA. This is to notify the product your company PHYTO SCIENCE SDN BHD is promoting for Stem Cell therapies with stem cell products such as Double Stemcell™ that is illegal & potentially harmful. With product DOUBLE STEMCELL™ company PHYTO SCIENCE SDN BHD has entered in consumer market has not been approved by DCA & was being studied under a clinical investigation only on animals that has been submitted to and allowed to proceed by DCA. Moreover come up with more hazardous counteracts on human body even can cause carcinogenic effects on the body & declared not to be fit for human consumption. The product is not safe and ineffective for its intended use as well. This is carrying the toxic effects so taking into account of all the investigation would like to advise to immediately cease this product & send your compliance in writing to this notice within 45 days of receipt of this letter.
Still on thwarting a unapproved product Double Stemcell™as stem cell treatments / therapies the authorities aggressively pursue the perpetrator who expose the Malaysian public to the dangers of unapproved stem cells and ensure that they are punished to the full extent of the law.

Thanks,

Mago Bint RU

Dato' Dr. Margo Azmie (Issuing Authority)

Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor, Malaysia

CONTACTS & MAP

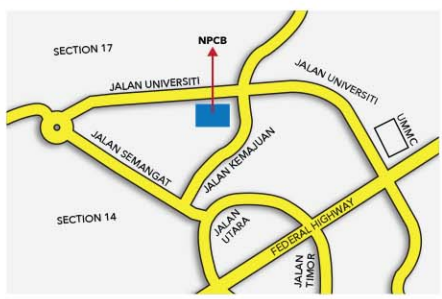
NATIONAL PHARMACEUTICAL CONTROL BUREAU (NPCB) **+ 603 - 7883 5400**

CENTRES	EXTENSION NO.
Centre for Product Registration – Deputy Director	**5487**
• Active Pharmaceutical Ingredient Section	8424
• Biotechnology Section	8423
• Complementary Medicine Section	8415
• Generic Medicine Section	5490
• New Drug Section	5522
• Regulatory Coordination Section	5502
• Veterinary Medicine Section	5500
Centre for Post-Registration of Products – Deputy Director	**5538**
• Cosmetic Section	5532
• Pharmacovigilance Section	5543
• Surveillance and Product Complaints Section	5552
Centre for Investigational New Product – Deputy Director	**5581**
• BE Centre & Ethics Committee Compliance Section	8403
• GCP Compliance Section	8401
• GLP Compliance Section	8404
• Investigational Product Evaluation Section	8406
• Investigational Product Safety Monitoring Section	8405
Centre for Compliance and Licensing – Deputy Director	**5564**
• GDP Section	5568
• GMP 1 Section	5566
• GMP 2 Section	5567
• Licensing and Certification Section	5569
• Quality and Industry Development Section	8556
Centre for Organisational Development – Deputy Director	**5553**
• Helpdesk	5560, 5561, 5562
• Information and Communications Technology Section	5555
• Quality, Competency & Communication Coordination Section	8481
Centre for Quality Control – Deputy Director	**5429**
• Bio-Pharmaceutical Testing Section	8894
• Complementary Medicines Testing Section	8892
• Laboratory Services Section	5431
• Pharmaceutical Chemistry Testing Section	8490
• Reference Standard Section	5468
• Research Section	8446
Centre for Administration	**8458**

NATIONAL PHARMACEUTICAL CONTROL BUREAU (NPCB),
MINISTRY OF HEALTH MALAYSIA
BIRO PENGAWALAN FARMASEUTIKAL KEBANGSAAN (BPFK),
KEMENTERIAN KESIHATAN MALAYSIA

Lot 36, Jalan Universiti,
46200 Petaling Jaya,
Selangor Darul Ehsan,
MALAYSIA
Tel : + 603 - 7883 5400
Fax : + 603 - 7956 2924

Website :
www.bpfk.gov.my



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