Newsletter of the Drug Control Authority, Malaysia

BERITA UBAT-UBATAN

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NEW DIRECTIVE

1. Directive 03/2013: Malaysian Variatian Guideline (MVG) for Pharmaceutical Products

A directive under Regulation 29 of the Control of Drugs and Cosmetics Regulations 1984 (Revised 2006) has been issued by the Senior Directive of Pharmaceutical Services, Dato' Eisah A. Rahman following decision made by the Drug Control Authority (DCA) in its 262nd Meeting on 28 March 2013.

With the implementation of this directive, product registration holders are required to follow the Malaysian Variation Guideline (MVG) which will bring changes to the processing time for variation application and evaluation.

Besides, a new type of variation is introduced namely the Minor Variation Notification (MiV-N). MiV-N provides flexibility to the industry in implementing variation first prior to notifying the National Pharmaceutical Control Bureau (NPCB). However, NPCB has the right to reject such notification if it does not fulfill the requirements such as conditions and supporting documents. The Minor Variation Prior-Approval (MiV-PA) involves changes with minimal impact on the aspects of safety, efficacy and quality of the product while the Major Variation (MaV) involves changes that may affect the safety, efficacy and quality of the product.

The variation application and evaluation for MiV-N (according to MVG) will be implemented from 1 July 2013. NPCB shall acknowledge receipt of a notification if the requirements as per described under MiV-N are fulfilled.

The variation application and evaluation for MiV-PA and MaV (according to MVG) will be implemented only in terms of the condition and documentation from 1 January 2014. The holders are given a period of 6 months to implement the approved variation.

The First Edition of MVG dated April 2013 is available on the NPCB website.

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ANNOUNCEMENTS

1) *Adjusting and Switching the Validity Period of Wholesale License for Registered Product to 'Calendar Year'*

Under Regulation 12, sub regulation (4), Control of Drugs and Cosmetics Regulations 1984, license issued shall be valid for one year. The current practice is that the validity period of wholesale license for registered product starts on 1 July and expires on 30 June of the following year.

Effective 2014, the wholesale license validity period will be adjusted to match the calendar year (similar as the manufacturing license and import license) which begins on 1 January and ends on 31 December of the same year. For the wholesale license application for 2013, the validity will be adjusted as follows:

No	Type of Application	Validity Period
a)	New Application	Valid till **31 December 2013**
b)	Renewal Application 2013/2014	**1 July 2013 – 31 December 2014**

2) *The Requirement to Register Food-Drug Interface Products that Contain Sea Cucumber / Gamat (Stichopus Sp.) as Active Ingredient*

The Food-Drug Interface (FDI) Committee Meeting between NPCB and Food Safety and Quality Division (BKKM) had decided that all FDI products containing sea cucumber (taken orally in any percentage) is classified as drug and needs to be registered with the DCA.

Therefore, companies involved in manufacturing, marketing or importing sea cucumber products (Stichopus Sp) that are not registered should submit their registration application through the NPCB online registration system.

3) *Abolishing the Issuance of Certificate of Registration / Sijil Perakuan Pendaftaran (SPP)*

Currently, under Regulation 8(8) of the Control of Drugs and Cosmetics Regulations 1984, the Drug Control Authority (DCA) is required to inform/notify the product registration holder regarding the approval of product upon DCA meeting.

Starting from 1 February 2013, the product registration holder for product in the Quest 3 System may refer to email notification upon approval by the DCA while the product registration holder for product in the Quest 2 System may refer to the list of new products approved by the DCA on NPCB's official website. Certificate of Registration will not be issued anymore as the Form A in the Regulations has been deleted since its amendment in 2006.

4) Stability Study Data (in Zone IV B) Requirements for Registered Pharmaceutical Products

According to the ASEAN Guideline on Stability Study of Drug Product, the application for product registration shall be supported with long-term stability testing data in Zone IV B (at 30°C ± 2°C/75%RH ± 5%).

The above requirement has been enforced for all new product registration applications since 2009. For applications submitted before 2009, the registration holders should ensure that the approval of variations for long-term stability study data in Zone IV B and updated product label (storage condition) is obtained before the submission of product renewal.

In addition, the requirement is applicable for all registered pharmaceutical products (scheduled and non-scheduled poison) except pharmaceutical products that require the cold-chain supply system. For products with active ingredients that are unstable in the Zone IV B, the holders are allowed to apply from DCA (with justification) for exemptions.

This requirement is effective from 1 January 2015.

SUMMARY OF PRESS RELEASES / ARTICLES

1. Consumers Cautioned against Using Cosmetic Products Containing Scheduled Poison

a) The public is advised to avoid buying and using the following cosmetic products:

No	Name of Products	Notification Number	Heavy Metal Detected	Notification Holder	Manufacturer
1.	Daily Protecting Cream – Joie et Beaute	NOT100778850K	Mercury	Rina Skincare (M) Sdn. Bhd.	ChiuMien Cosmetics Co., Ltd, Taiwan
2.	Yoko Whitening Cream Ginseng & Pearls	NOT100901081K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand
3.	Yoko Whitening Cream with SPF-15	NOT100901085K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand
4.	Yoko Yogurt Milk Whitening Cream	NOT100901088K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand
5.	Yoko Beauteen Sunflower Whitening Cream	NOT100901094K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand
6.	Yoko Freckle Cream	NOT100901098K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand
7.	Yoko Whitening Cream	NOT100901107K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand
8.	Yoko Whitening Cream Aloe Vera Extract	NOT100903039K	Mercury	PK-1 Wholesales Trading Sdn. Bhd.	Siam Yoko Co. Ltd, Thailand

The product notifications of the cosmetics above have been cancelled following the detection of the heavy metal mercury.

Mercury is prohibited in cosmetic products due to its potential hazard on human health. Mercury compounds are readily absorbed through the skin on topical application and tend to accumulate in the body. Direct and prolonged exposure to mercury can cause damage to the brain, nervous system and kidneys. Using products containing mercury can also result in skin rashes, irritation, and other changes to the skin.

Anyone who is in possession of this product is advised to immediately cease selling / distributing / using it. The possession of this product is an offence under the Control of Drugs and Cosmetics Regulations 1984.

b) The public is advised to avoid buying and using the following cosmetic products:

No	Name of Products	Notification Number	Scheduled Poison Detected	Notification Holder	Manufacturer
1.	Acrena Pure Herbal Papaya Soap	NOT100802337K	Tretinoin	Haresh Enterprises Sdn. Bhd.	Re-X Products Co., Ltd, Thailand
2.	White Complex	NOT100801451K	Tretinoin	NB Natural Beauty Facial & Slimming (uda) Sdn. Bhd.	Cyclin Cosmetic Sdn. Bhd.
3.	SS Pearl Cream	NOT110602236K	Mercury	Shin Viky Beauty Global	Kingou (International) Cosmetics Co. Ltd, China
4.	SS Vita C Night Repair	NOT110602264K	Mercury	Shin Viky Beauty Global	Kingou (International) Cosmetics Co. Ltd, China

All cosmetic products mentioned above are no longer allowed to be sold in Malaysia.

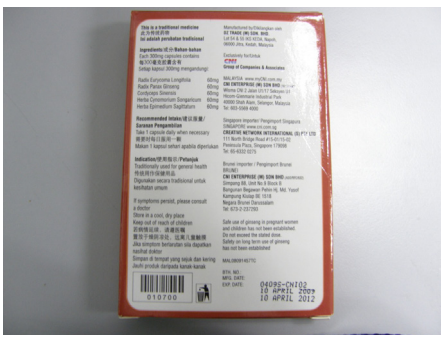
The use of tretinoin in cosmetic products is also prohibited. Cosmetics adulterated with tretinoin are commonly found in products used for acne treatments or to improve skin conditions. Preparations containing tretinoin should only be used under the supervision of healthcare professionals. The unsupervised usage of tretinoin may cause redness to the skin, discomfort, stinging, peeling and skin becomes sensitive to sunlight.

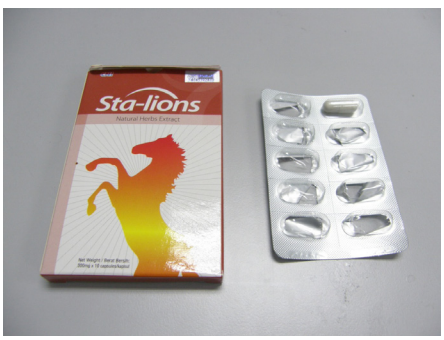
The companies responsible for placing these products in the market have been instructed to immediately halt the sale and supplies of the product mentioned and remove all physical stocks from the market within 72 hours.

2. Cancellation of Registration of Traditional Product : Sta-lions

The public is advised to avoid buying and using traditional product Sta-lions (MAL08091457TC). The registration of this product has been cancelled by the DCA at its 262nd meeting on 28 March 2013 following the detection of scheduled poison tadalafil. This product was registered with the indication of traditional use for general health.

Tadalafil is used to treat erectile dysfunction (ED) or impotence and can only be supplied by doctors or be obtained at pharmacies upon prescription. Usage of tadalafil without proper diagnosis and monitoring by doctor may cause serious adverse events such as decreased or loss of vision and hearing, lowering of blood pressure to dangerous level and cardiovascular events such as stroke and heart attack (myocardial infarction). Tadalafil or its analogues are not allowed to be formulated in any product classified as traditional product. Therefore, this product may potentially cause detrimental effects especially to those who are at higher risk of developing such adverse events like heart patients (angina pectoris) receiving nitrates.





Consumers are advised to stop using Sta-lions and they shall seek further advice from healthcare professionals, if experiencing any unpleasant effects or adverse events.

Anyone who is in possession of this product is advised to immediately cease selling, distributing or using it. The possession for sale of these products is an offence under the Control of Drugs and Cosmetics Regulations 1984.

3. Response to Newspaper Article 1

SIN CHEW DAILY (27th FEBRUARY 2013)
"THREE UNREGISTERED HEALTH SUPPLEMENT PRODUCT, SUSPECTED FROM MALAYSIA AND D INDONESIA. TWO GOT SERIOUS ADR"

The Health Sciences Authority (HSA) Singapore has issued a warning on 26 February 2013 regarding three traditional products that have been found to contain adulterants. The public is advised not to buy or use these products.

Two patients suffered adverse reactions of Cushing's syndrome after taking Ginseng Baji Gu Ci Wan and Tu Chong Ginseng Wan Le Seang respectively which have been found to contain

dexamethasone and chlorpheniramine. Meanwhile, another adulterated product, X-Tract Nature contains prednisone, phenylbutazone, chlorpheniramine and paracetamol.

Dexamethasone and prednisone are very potent corticosteroids used for anti-inflammatory purposes. Unsupervised long-term use can cause increased blood glucose level, high blood pressure, bone disorders, increased risk of infections and Cushing's syndrome. Phenylbutazone is a non-steroidal anti-inflammatory drug (NSAID) that is not available in Malaysia since its risk of causing serious adverse events have been assessed to outweigh its benefits. Long term use of paracetamol without appropriate supervision may cause kidney or liver damage.

Chlorpheniramine is an antihistamine used to relieve allergic reactions with the possible side effects of drowsiness, confusion and urinary retention.

Based on the review, the three products are not registered with the DCA. The registration number MAL20032388TC printed on the product label for Ginseng Baji Gu Ci Wan is also found to be faked. To date, no complaints or adverse drug reactions from the use of these products have been reported.

The public is advised not to buy or use product that is not registered with the DCA since its quality and safety is not guaranteed.

4. Response to Newspaper Article 2

SIN CHEW DAILY (1st MAY 2012, Page 29)
"HONG KONG RECALLED UNREGISTERED MEDICATION"

According to the local newspaper article stated above, the Department of Health Hong Kong had ordered the company Yuen Hui Trading Co. to recall their product, Lorista Tablets 50mg (Registration No. : HK-59349) due to the discovery of non-approved package insert supplied with this product. Subsequently, the product was classified as a non-registered product in Hong Kong.

Lorista Tablet 50mg is a product registered with the DCA since March 2011. However, this product has not been marketed in Malaysia to date. Therefore, Malaysia is not involved with the recalling of such product as reported in Hong Kong.

5. Response to Newspaper Article 3

CHINA PRESS (1st FEBRUARY 2013)
"FRANCE BANNED THE SALE OF ORAL CONTRACEPTIVE PILLS WHICH CAUSED 4 DEATHS"

On 30 January 2013, The French National Agency of Medicine and Health Products Safety (ANSM) had issued a statement regarding their action to suspend the product registration of

Diane 35 and its generics. This decision was made following a study which found that the risk of using Diane 35 outweighs its benefits. The latest safety data shows that the risk of blood vessel blockage (thrombosis) is four times higher in women who receive treatment with this drug.

Diane 35 is a combination product that contains the active ingredient Cyproterone acetate 2mg and ethinylestradiol 0.035mg. In Malaysia, Diane 35 and four generics have been registered by the DCA with the indication of treating androgen dependent disease in female patients such as serious acne, seborrhea, inflammation or formation of nodules, androgenetic alopecia and mild hirsutism. It is not indicated for pregnancy prevention treatment. The most common side effects include vomiting, abdominal pain, headache, weight gain, rashes and mood swings.

According to NPCB's Adverse Drug Reaction Monitoring Program, there were seven reports of adverse events involving the use of Diane 35 to date. However, there was no report of blood vessel blockage.

The DCA will continue monitoring this issue and review the use of Diane 35 in the treatment of acne. Women who are taking Diane 35 are advised to consult health professionals for alternatives should they encounter or experience any adverse events.

6. Response to An Article in The Wall Street Journal

THE WALL STREET JOURNAL (14th JANUARY 2013)
"MERCK PULLS CHOLESTEROL DRUG TREDAPTIVE"

According to The Wall Street Journal, Merck & Co. had announced that it is discontinuing the sales of cholesterol drug, Tredaptive (niacin/laropiprant). The Pharmacovigilance Risk Assessment Committee (PRAC), advisory committee for The European Medicines Agency (EMA), recommended for the drug to be withdrawn from the market after preliminary trial results showed that Tredaptive failed to significantly reduce the risk for heart attacks and strokes. Moreover, some of the trial subjects experienced side effects such as gastrointestinal bleeding.

In Malaysia, the DCA had received product registration application for Tredaptive tablet (niacin 1g / laropiprant 20mg) from Merck Sharp & Dohme (I.A.) Corp. Malaysia (MSD) in September 2009. However, the DCA had rejected the application as a result of:

i) Insufficient clinical data on the physiological effects and long-term safety of laropiprant
ii) Insufficient data on the efficacy and long-term safety for cardiovascular risk, hepatic injury and psychiatric adverse effects
iii) The real-time stability data submitted by the manufacturer (to support the life expectancy for 24 months at 30°C/65% RH) is incomplete.

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CENTRES	EXTENSION NO.
Centre for Product Registration – Deputy Director	5487
• New Drug Section	5522
• Generic Medicine Section	5490
• Biotechnology Section	8423
• Complementary Medicine Section	8415
• Active Pharmaceutical Ingredient Section	8424
• Veterinary Medicine Section	5500
• Regulatory Coordination Section	5502
Centre for Post-Registration of Products – Deputy Director	5538
• Surveillance and Product Complaints Section	5552
• Pharmacovigilance Section	5543
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Centre for Organisational Development – Deputy Director	5553
• Information, Communication & Technology Section	8577
• Helpdesk	5561
Centre for Quality Control – Deputy Director	5429
• Bio-Pharmaceutical Testing Section	8457
• Research and Development Section	8448
• Pharmaceutical Chemistry Testing Section	5462, 5456, 5450
• Laboratory Services Section	5431
• Natural Product Testing Section	5471
• Reference Standard Section	5468
Centre for Administration	8458

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