BERITA UBAT-UBATAN

Volume 66 | No.45 | ISSN 0128-0627

EVENTS

National Pharmaceutical Control Bureau (BPFK) adopts new name as the

National Pharmaceutical Regulatory Agency (NPRA)

The National Pharmaceutical Control Bureau (BPFK) is changing its name in accordance with the restructuring program of Pharmaceutical Services, Ministry of Health (MOH) which was approved by the Public Service Department (PSD) officially on April 1, 2016. The organization of regulatory-based instituition founded in 1978 will now be known as the National Pharmaceutical Regulatory Agency, as announced on July 15, 2016 officiated by YB Datuk Seri Dr. S. Subramaniam.

FULL REPORT ON PAGE 2

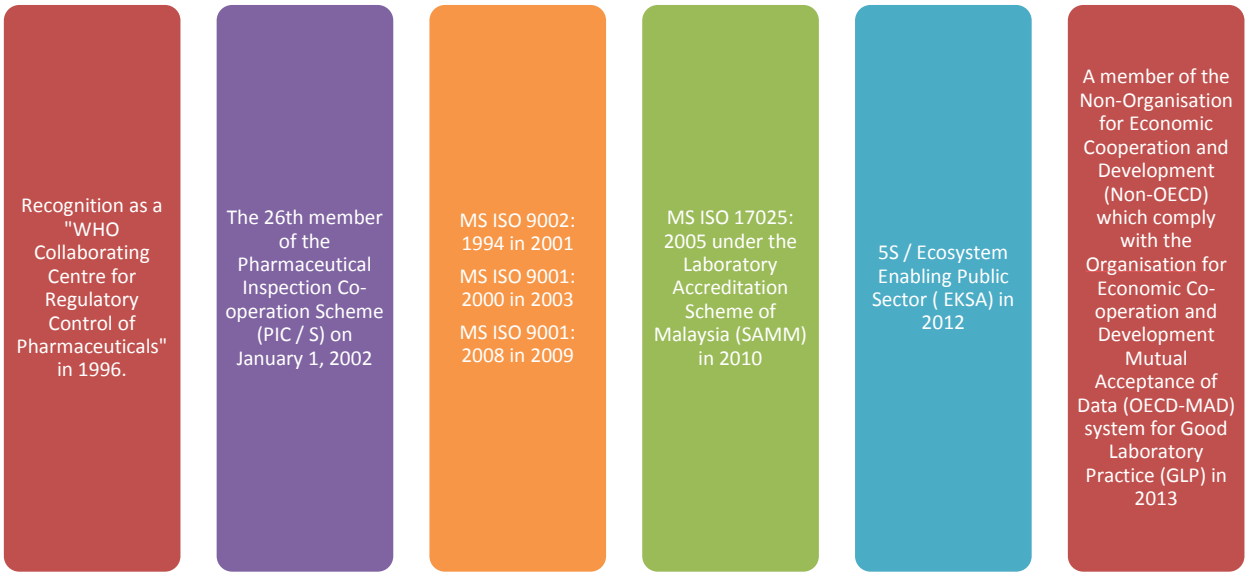
IN THIS ISSUE

DCA EDITORIAL TEAM

The rebranding of this institution is to reflect the organisation's focus on collaboration among employers to improve regulations, and to rationalise to its key stakeholders, including the ministry of health, pharmaceutical companies and vendors. The National Pharmaceutical Regulatory Agency (NPRA) will become an independent regulatory agency in Malaysia, which is responsible for ensuring the quality, efficacy and safety of pharmaceutical products, namely products to prescription drugs, supplements , 'over the counter' product, traditional, cosmetic and veterinary medicine.

In 2015, a total of 1,220 products were registered, which consists of prescription products, non-prescription, natural, veterinary and health supplements. This year, as of March 2016, a total of 214 products have been registered. The number of products that are registered until March 2016 stood at 23.735 products. While revenue in 2015, a total RM12,433,355.67 was obtained, and revenue collection for this year is expected to increase in line with the imposition of fees for existing activities and expansion of new activities undertaken by NPRA.

As the only regulatory agency to control for such products to be registered with expertise and important role performed by it, various achievements and recognition were received both locally and internationally. These include, among others:



This achievement clearly illustrates how NPRA, as a government department, has grown rapidly since it was established in 1978. Since its inception, the department has gone through many transformations in order to develop a regulatory agency that is comparable with other international regulatory agencies. In this aspect, NPRA also works closely with various parties including industry, academia, stakeholders, departments - government departments, local agencies and agencies abroad through various forums including, among others, dialogue and discussions, meetings - meetings and so on.

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

1. ***Directive No. 7 Year 2016 [Ref: (38) dlm. BPFK/PPP/07/25]: Safety updates in product package insert and RiMUP pertaining to the Risk of Osteonecrosis of the External Auditory Canal for All Products Containing Bisphosphonate (Alendronate, Clodronate, Ibandronic Acid, Pamidronate, Risedronate, Zoledronic Acid).***

Following the decision made by the Drug Control Authority (DCA) in its 299th Meeting on 28th April 2016, this directive was issued to enforce the said safety updates. The following safety updates shall be included in package insert and RiMUP of all products containing Bisphosphonate (Alendronate, Clodronate, Ibandronic Acid, Pamidronate, Risedronate, Zoledronic Acid):

Special Warnings and Precautions for Use: *(In package insert)*

Osteonecrosis of the external auditory canal

Osteonecrosis of the external auditory canal has been reported with bisphosphonates, mainly in association with long-term therapy. Possible risk factors for osteonecrosis of the external auditory canal include steroid use and chemotherapy and/or local risk factors such as infection or trauma. The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms including chronic ear infections.

Adverse Drug Reactions: *(In package insert)*

Very rare: Osteonecrosis of the external auditory canal (bisphosphonate class adverse reaction).

Possible Side Effects: *(In RiMUP)*

Very rare: Talk to your doctor if you have ear pain, discharge from the ear, and/or an ear infection. These could be signs of bone damage in the ear.

Effective date of this safety updates package insert is as follows:

New registration and products under evaluation: **1st July 2016**
Registered products: **1st January 2017**

The said safety updates for the registered products shall be done via variation application. This directive came into force starting from **1st July 2016.**

2. ***Directive No. 8 Year 2016 [Ref: (39) dlm. BPFK/PPP/07/25]: Evaluation on examination reports from Bioequivalence (BE) Studies Centre for product registration***

Following the decision made by the Drug Control Authority (DCA) in its 300th Meeting on 7th June 2016, this directive was issued to expand the scope of evaluation on examination report for bioequivalence (BE) study centres for the purpose of product registration.

Examination report assessment for bioequivalence (BE) studies from other regulatory bodies recognized by the BPFK is accepted including:

1. United States of America, Food and Drug Administration (USFDA)
2. European Medicines Agency (EMA)
3. Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom
4. French National Agency for Medicines and Health Products Safety (ANSM)
5. Federal Institute for Drugs and Medical Devices (BfArM),.Germany
6. Austrian Agency for Health and Food Safety (AGES)
7. Other European regulatory bodies depending on the scope of evaluation that had been conducted.

The product in the BE examination reports must be the same product to be registered in Malaysia. In the case of unsatisfactory evaluation upon the examination report, the application will be rejected.

This directive came into force starting from **1st July 2016.**

3. ***Directive No. 9 Year 2016 [Ref : (40) dlm. BPFK/PPP/07/25]: Requirement of Good Laboratory Practice (GLP) for non-clinical safety studies for the purpose of product registration for New Chemical Entity (NCE), Biologics and Herbs with high therapeutics claims***

Following the decision made by the Drug Control Authority (DCA) in its 300th Meeting on 7th June 2016, this directive was issued to implement the above said requirement.

Non-clinical safety studies conducted for the purpose of product registration in Malaysia shall be conducted in non-clinical study facilities that are listed in the GLP Compliance Monitoring Programme of National Pharmaceutical Regulatory Agency (NPRA) or have the status of GLP compliance from the National Compliance Agency of OECD member countries or Non-OECD member adhering to Mutual Acceptance of Data on GLP.

For data on non-clinical safety studies for the purpose of product registration: -

1. Each non-clinical safety study shall be submitted together with a full report (final report) on safety study.
2. Only full reports of non-clinical research facilities listed in the GLP Compliance Monitoring Programme of NPRA or National Compliance Agency of OECD member countries or Non-OECD member adhering to Mutual Acceptance of Data on GLP will be accepted for registration purpose.
3. Acceptance of full report of non-clinical safety study is subjected to the outcome of NPRA evaluation.

This directive came into force starting from **1st January 2018.**

4. Directive No. 10 Year 2016 [Ref : (41) dlm. BPFK/PPP/07/25]: Enforcement of Plasma Product Lot Release for All Plasma Product Registered in Malaysia

Following the decision made by the Drug Control Authority (DCA) in its 300th Meeting on 7th June 2016, this directive was issued to enforce the Plasma Product Lot Release activity for all plasma products registered in Malaysia.

Any registered plasma products found incompliance with the requirements of the Plasma Product Lot Release in Malaysia:

a) The plasma product should not be distributed for the usage of the Malaysian citizen.

b) The plasma products must be disposed within Malaysia.

c) The evidence of collection the purpose of disposal must be submitted by the Registration Holder to BPFK within 30 days from the date of Notification of Non - Compliance issued.

d) Proof of the disposal must be submitted by the Registration Holder to BPFK within 90 days from the date of collection for disposal.

Failure of the Import Licence and Wholesale License Holder appointed by the Registration Holder to comply with the requirement of Good Distribution Practice (GDP), may lead to revocation of the licence as a punitive action. In case of non-compliance, it is the responsibility of the Registration Holder to have a contingency plan to ensure that the supply of plasma products in Malaysia are not affected.

This directive came into force starting from **1st July 2016.**

5. *Directive No. 11 Year 2016 [Ref : (42) dlm. BPFK/PPP/07/25]: Acceptance of Good Manufacturing Practices (GMP) compliance validation for the purpose of registration renewal of pharmaceutical products registered with the Drug Control Authority*

Following the decision made by the Drug Control Authority (DCA) in its 300th Meeting on 7th June 2016, this directive was issued to inform the acceptance of Good Manufacturing Practices (GMP) compliance validated by competent authority of the country of reference to be recognized as a condition of registration renewal of registered pharmaceutical products.

Starting from **1st January 2017**, for the purpose of re-registration/renewal of registered pharmaceutical product manufactured in any non-PIC/S country that has been inspected by the following competent authority from recognized reference countries, the GMP certificate/document issued by the said Authority is accepted.

I. PIC/S participating member countries involved in the formation of Pharmaceutical Inspection Convention (PIC) between the year 1970 and 1993;

Austria, Denmark, Finland, Iceland, Liechtenstein, Norway, Portugal, Sweden, Switzerland, United Kingdom, Hungary, Ireland, Romania, Germany, Italy, Belgium, France, Australia.

Total: 18 Countries

II. Members of PIC/S who are also the European Union (EU) or European Free Trade Association (EFTA) members that have acceded to the European Economic Area (EEA):

I. EU (EEA):
Austria*, Belgium*, Cyprus, Czech Republic, Slovakia, Germany*, Denmark*, Estonia, Finland*, France*, Hungary*, Ireland*, Italy*, Lithuania, Latvia, Malta, Netherland, Poland, Portugal*, Romania*, Sweden*, Slovenia, Slovak Republic, Sepanyol, United Kingdom*, Greece

II. EFTA (EEA):
Norway*, Liechtenstein*, Iceland*

Note:* Countries that also are members of PIC.
The list of countries under EEA are subject to change.

Total: 13

III. The competent authority from reference countries stated in the Drug Registration Guidance Document (DRGD) for registration of pharmaceutical products :

United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan and Switzerland

Note : The underlined countries are the PIC or EEA countries.

Total: 3

IV. Any competent authority that has a cooperation agreement such as Mutual Recognition Agreement (MRA) with PIC/S or any reference countries stated under I and II above

Example: European Medicines Agency (EMA) dan PIC/S.

The requirement of GMP inspections conducted by the DCA imposed on the manufacturers of pharmaceutical products in country which is not a PIC/S member including those that had been audited by the competent authorities of other PIC/S countries for the purpose of new registration remains unchanged as enshrined in the Directive No. 1 Year 2016 which came into force on **1st July 2016**.

With the implementation of this directive, the paragraph 1.2 in the Directive No. 1 Year 2016 is automatically voided.

6. ***Directive No. 12 Year 2016 [Ref : (43) dlm. BPFK/PPP/07/25]: Use of the new Drug Registration Guidance Document (DRDG) Second Edition, September 2016***

This directive was issued to implement the use of the newly Drug Registration Guidance Document (DRDG) 2016 Second Edition for all applicants and product registration holders of pharmaceutical products, health supplements and natural products in Malaysia. The DRDG 2016 Second Edition is available through the NPRA official website at www.npra.gov.my.

This directive came into force starting from **1st September 2016.**

7. ***Directive No. 13 Year 2016 [Ref: (44) dlm. BPFK/PPP/07/25]: Warning Statements Update on Product Label Regarding the Risk of Respiratory Problems/ Shortness of Breath for all products that contains active ingredients of "Minyak Cajuput" (Melaleuca Leucadendra) in Topical Dosage Form.***

Following the decision made by the Drug Control Authority (DCA) in its 301st Meeting on 30 June 2016, this directive was issued to enforce the said warning statements update.

The following warning statements concerning the risk of respiratory problems / shortness of breath shall be added to label of all products that contain active ingredients of *Minyak Cajuput* (*Melaleuca leucadendra*) : -

Warnings:

Bahasa Malaysia: -
Produk ini tidak boleh disapu pada muka, khususnya di kawasan hidung bayi dan kanak-kanak. Ia mungkin boleh menyebabkan masalah pernafasan / kesukaran bernafas.

English: -
This product should not be applied to the facial area, in particular around the nose of infants and small children. It might cause breathing problem / shortness of breath.

The implementation dates for the warning statements update on product label of all products containing active ingredients of *Minyak Cajuput* (*Melaleuca leucadendra*) are as follows:

New registration and products under evaluation: 1st August 2016

Registered Products: 1st January 2017

The said warning statements update for the registered products shall be done via variation application.

This directive came into force starting from **1st August 2016.**

4. Directive No. 14 Year 2016 [Ref: (45) dlm. BPFK/PPP/07/25]: Implementation of Malaysian Variation Guideline for Natural (Traditional Medicine & Homeopathy) and Health Supplement Products (Abridged Evaluation)

Following the decision made by the Drug Control Authority (DCA) in its 301st Meeting on 30 June 2016, this directive was issued to enforce the use of Malaysian Variation Guideline for Natural (Traditional Medicine & Homeopathy) and Health Supplement Products (Abridged Evaluation).

A total of 37 types of variation as follows are contained in the guideline:

- 13 Major Variation (MAV)
- 16 Minor Variation-Prior Approval (MIV-PA)
- 8 Minor Variation-Notification (MIV-N)

Below is are the processing timelines for the three (3) types of variation:

Type of Variation	Processing Time
Minor Variation Notification (MiV-N)	• Product registration holders are given the flexibility to implement changes without having to seek prior approval of NPRA, provided that they meet all the requirements set. • Product registration holder is made compulsory to make a notification regarding the changes that have been implemented to NPRA where NPRA will approve the notifications received, within 7 working days. • Notification application can be rejected if it does not meet the requirements where the product registration holder shall cease all the changes that have been implemented.
Minor Variation Prior Approval (MiV-PA)	• Approval (if all requirements are met) or the first correspondence (if requires additional data) will be issued to product registration holder within 30 working days. • Approval (if all requirements are met) or subsequent correspondence

	will be issued within 20 working days. • Applications may be rejected if the product registration holder does not respond within 20 working days from the date of the correspondence. • The application will also be rejected if the requirements are still not met after the second correspondence.
Major Variation (MaV)3	• Approval (if all requirements are met) or the first correspondence (if requires additional data) will be issued to product registration holder within 45 working days. • Approval (if all requirements are met) or subsequent correspondence will be issued within 30 working days. • Applications may be rejected if the product registration holder does not respond within 30 working days from the date of the correspondence. • The application will also be rejected if the requirements are still not met after the second correspondence.

The grace period of implementation by the product registration holder after variation application is approved is 6 months. This directive came into force starting from **1st August 2016.**

TRADITIONAL PRODUCTS / HEALTH SUPPLEMENTS

A) *Caution on Using Traditional Products Containing Scheduled Poisons*

The National Pharmaceutical Control Bureau (NPCB) would like to urge the public to refrain from buying and using a traditional product labeled as **"El Biozing**" which had been found to contain dexamethasone, a scheduled poison.

Product Name	Registration Number	Adulterant Detected	Product Registration Holder and Manufacturer
El Biozing	MAL10070646TC	Dexamethasone	Lagenda Organic Biotech Sdn Bhd, Kelantan

El Biozing is registered as a traditional product for men's and women's health and to strengthen the body. However, this product has been promoted in the market by its distributor Penawar Lagenda Marketing with various unapproved health claims includes strengthening muscles and bone and for joint pain relief. Members of the public who are using El Biozing product are advised to **IMMEDIATELY** consult a doctor before stopping. A Sudden discontinuation of taking products that contain corticosteroid without proper medical supervision can cause serious withdrawal symptoms such as weakness, confusion, and low blood pressure, especially for users who have been taking this product for more than a few weeks.

Registration of this product has been cancelled by the Drug Control Authority (DCA) at its 290th meeting on 3rd of August 2015. Any scheduled poison is not allowed to be formulated in a product which is classified as a traditional product under the Sale of Drug Act 1952 and Control of Drugs and Cosmetics Regulations 1984. All sellers are warned to stop sales and distribution of this product. Individuals who commit an offence under these laws will face penalty up to a period up to three (3) years for the first offence, and penalty up to RM50,000 and or imprisonment for a period up to five (5) years for a subsequent offence. A company found guilty can be fined up to RM50,000 for the first offence and a fine of up to RM100,000 for a subsequent offence.

B) *Caution on Using Unregistered Traditional Products Containing Scheduled Poisons*

The National Centre for Adverse Drug Reactions Monitoring, NPCB would like to remind the public not to buy or use the following unregistered products:

Product Name	Registration Number	Adulterant Detected	Description
Hai Leng Hai Beh (Herbal Itch Removing Capsule)	MAL05052021TC (Fake)	Dexamethasone Chlorpheniramine Paracetamol	Brownish Pill
Dong Mai Tan	MAL20013016T (Fake)	Dexamethasone	Black Pill
Seven Leave Ginseng	MAL19984210T (Fake)	Dexamethasone	Black Pill

The traditional product labelled as " Hai Leng Beh" was found to contain adulterants of dexamethasone, chlorpheniramine and paracetamol that can cause serious side effects. A report of adverse effects of weight gained and moon face from a consumer following the oral intake of the product for about two months to treat skin irritations.

At the same time, the traditional product labelled as *Dong Mai Tan and Seven Leave Ginseng were also proven to contain* dexamethasone after sampling of the product were made through adverse reaction reports received by the National Centre for Adverse Drug Reactions Monitoring (NPCB). The NPCB received a total of four (4) reports of adverse events product involving Dong Mai Tan and eight (8) reports of adverse events involving Seven Leave ginsengs product. Among them, serious adverse events reported are liver failure and Cushing's syndrome which is characterized by a round face (moon face) and weight increase with obesity in the central part of the body (central obesity).

Dexamethasone and chlorpheniramine are controlled under the Poisons Act 1952. Dexamethasone is a potent corticosteroid and used for the treatment of swelling and serious inflammation problems. Long term unsupervised use of dexamethasone can lead to serious side effects that can be harmful to health such as muscle weakness, bone loss, increased in blood sugar levels leading to diabetes, high blood pressure, glaucoma and an increased risk of infections. Consumer can also experience Cushing's syndrome which is characterized by a rounded face and enlarged upper part of body but shrinkage of arms and legs. Patients with chronic diseases such as diabetes, poses higher risk and are advised not to use unregistered items as they may be adulterated with corticosteroids. Corticosteroids can cause uncontrolled blood sugar levels and therefore cause serious complications. Whereas, Chlorpheniramine is used to relieve colds and allergic reactions such as rashes. Chlorpheniramine side effects include drowsiness, blurred vision, vomiting, constipation and weakness of limbs coordination.

The public is advised not to buy or consume products that are not registered with the DCA or with fake registration number as their quality and safety are not known.

CONTACTS & MAP

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CENTRES	EXTENSION NO.
Centre for Product Registration – Deputy Director	ONE-STOP CALL CENTRE 5511
• Active Pharmaceutical Ingredient Section	
• Biotechnology Section	
• Complementary Medicine Section	
• Generic Medicine Section	
• New Drug Section	
• Regulatory Coordination Section	
• Veterinary Medicine Section	
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

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