Newsletter of the Drug Control Authority, Malaysia

BERITA UBAT-UBATAN

VOLUME 51 • No. 29 • ISSN 0128-0627 March 2011

DIRECTIVES & GUIDELINES

1. Three directives under Regulation 29 of the Control of Drugs and Cosmetics Regulations 1984 (Revised 2006) have been issued by the Senior Director of Pharmaceutical Services, Dato' Eisah A. Rahman following decisions made by the DCA during its 236th and 237th meeting on 27th January 2011 and 17th March 2011 respectively.

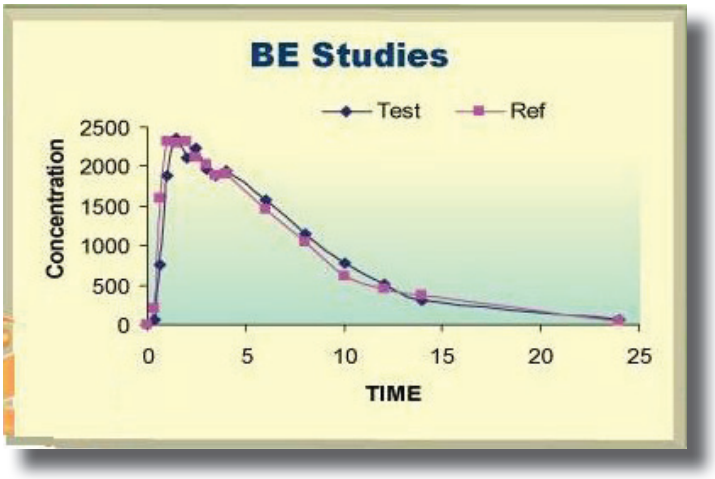
a) Directive 01/2011: Enforcing the Requirement of Bioequivalence (BE) Studies for All Immediate Release, Oral, Solid Dosage Form Generic Products Containing Scheduled Poison as Active Ingredients as well as Accreditation of BE Research Centres

The DCA had imposed on Bioequivalence (BE) studies requirement for all immediate release, oral, solid dosage form generic products containing scheduled poison as Active Ingredients as well as accreditation of BE research centres. This requirement will be implemented starting 1st January 2012.

Bioequivalence

Two drug products are considered bioequivalent if they are pharmaceutically equivalent and their bioavailabilities after administration in the same molar dose are similar to such a degree that their effects, can be expected to be essentially the same.

For registered generic products containing scheduled posion as active ingredients, the BE studies report must be submitted during the application for product registration renewal (for product registration that expires after 31st December 2012).



The accreditation of local BE research centers in terms of compliance with Good Clinical Practice and Good Laboratory Practice will be fully enforced in 2012. In addition, inspection of foreign research centres will be carried out starting 2012.

All product registration holders are instructed to submit BE studies report for their registered products according to the specified dates and any failure in submission will result in product de-registration.

IN THIS ISSUE

DCA EDITORIAL TEAM

b) Directive 02/2011: Data Exclusivity (DE) in Malaysia

The Directive on DE is issued by the Director of Pharmaceutical Services and shall come into force on **1st March 2011.**

All registration holders are instructed to comply to the requirements below:

Data exclusivity (DE) in Malaysia

Objective

To protect the undisclosed, unpublished and non-public domain pharmaceutical test data, the origination of which involves a considerable effort, submitted as required to the Director of Pharmaceutical Services for the purpose of scientific assessment.

Application

This Directive is applicable to

i) *New drug product containing a New Chemical Entity (NCE)*

ii) *Second indication of a registered drug product*

Grant of DE

Any person may apply for DE by submitting documents to the Director of Pharmaceutical Services.

An application shall only be considered for:

i) *New drug product containing NCE is made within 18 months from the date the product is first registered or granted marketing authorisation;*

ii) *Second indication of a registered drug product is made within 12 months from the date the second indication is approved;*

AND granted DE/ Test Data Protection

For a registered new drug product containing NCE that has been granted DE, registration of any other drug product with the same active moiety as the registered drug product can be considered if the applicant:

i) *Provides pharmaceutical test data to demonstrate Quality, Safety and Efficacy pf the drug product; OR*

ii) *Has obtained consent in writing for right of reference or use of the test data from an authorized person.*

Period

The period of the DE shall not be more than:

i) *5 years for a new drug product containing NCE*

ii) *3 years for a second indication of a registered drug product*

Appeal

Any person may make a written appeal to the Minister within 14 days from the date the decision is made known to him and the Minister's decision shall be final.

Supporting data or documents may be submitted not later than:

i) *120 days for application of new products containing any NCE*

ii) *90 days for application for second indication of a registered product*

**Definition of terms used in the application of DE and the non-application of DE are mentioned in the full instruction which is downloadable from our website at http://www.bpfk.gov.my/*

c) *Directive 03/2011: Implementation of Regulatory Control of Active Pharmaceutical Ingredients (API) in Malaysia*

A significant part of the quality of a finished pharmaceutical product is dependent on the quality of the Active Pharmaceutical ingredients (APIs) used for its formulation. Therefore, a proper system of qualification of suppliers is necessary to ensure a constant sourcing of APIs of appropriate quality and to safeguard the public health interests. This will be done through standardised quality assessment and inspection procedures.

The directive has been issued together with the guideline for Regulatory Control of APIs to implement regulatory control of Active Pharmaceutial Ingredients (API) by imposing additional technical data regarding API as part of the requirements in new drug product registration application. The technical requirements of the API is to be submitted during product registration application where the evaluation is carried out simultaneously with the assessment of product dossier.

The regulatory control of APIs will be implemented prospectively in stages with voluntary submission of technical data regarding API for New Chemical Entities (NCE) in April 2011 followed by a mandatory implementation on 1st January 2012. The date of implementation for submission of technical data regarding API of generic pharmaceutical products (including both scheduled poison and non-scheduled poison) will be determined later.

The submission shall be done online and the procedure is similar to that of existing product registration. No processing fee will be charged for API evaluation as the API application is already incorporated in the application for product registration.

What is an API?

Any substance or mixture of substances intended to be used in the manufacture of a drug product and that when used in the production of a drug becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effets in the diagnosis, cure, mitigation, treatment or prevention of diseases, or to affect the structure and function of the body.

API can be classified into:

- Inorganic substances;
- Organic substances (isolated from materials of animal or human origin); and
- Organic substances (synthetic or semi-synthetic or isolated from herbal sources or micro-organisms)

The procedure for control of APIs is based on the following principles:

i) A general understanding of the production and quality control activities of the manufacturer;

ii) Assessment of API data and information, including changes and variations, submitted by the MAH/API manufacturer. These data should include the manufacturing process, material specifications and test data and results;

iii) Assessment of the manufacturing site(s) for consistency in production and quality control of raw materials, with specific emphasis on key raw materials and APIs during and after purification through compliance with Good Manufacturing Practice (GMP);

iv) Random sampling and testing of APIs (post marketing surveillance);

v) Handling of complaints and recalls;

Scope of API Regulatory Control Guideline

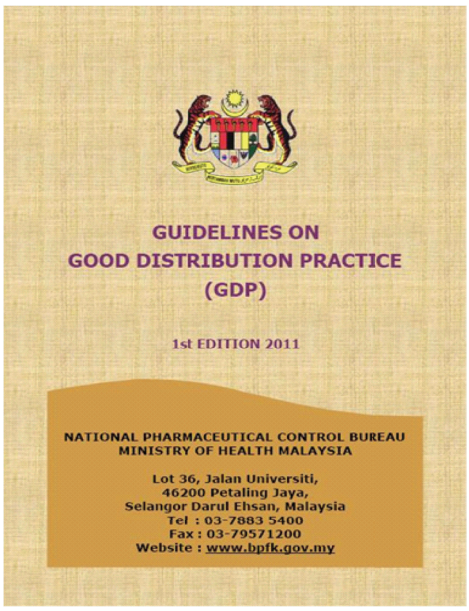
- *The guideline encompasses the APIs of new products for registration. This is applicable to all pharmaceutical products (excluding traditional products, veterinary products, and health supplement products) both locally manufactured and imported.*
- *Biological active substances and immunological active substances are excluded from the scope of this guideline.*
- *APIs used in products for export only (FEO) are exempted from the requirement for submission of the Drug Master File (DMF) and Certification of Suitability (CEP) in the product application.*
- *The DMF and CEP are only applicable for final APIs and not API intermediates.*

- *Separate registration of the APIs is not a requirement for the purpose of product registration. However, the required technical documentation pertaining to each API should be submitted with the new online product registration application.*
- *Assessment of an API will be performed once submission of an application for registration of a product using the said API is made by a Marketing Authorization Holder (MAH).*

2. *Guidelines on Good Distribution Practice (GDP)*

Definition of GDP

"The measures that need to be considered in the storage, transportation and distribution of any registered product or notified cosmetic and its related materials such that the nature and quality intended is preserved when it reaches the consumer."



The NPCB had released the 1st Edition of Guidelines on Good Distribution Practice (GDP) in January 2011. This guideline is used as a standard to justify status and as a basis for the inspection of facilities, such as manufacturers, importers and wholesalers.

All manufacturers, importers and wholesalers of registered products or notified cosmetics and its related materials are required to adopt proper distribution and store management procedures appropriate for the distribution and storage of products or cosmetics and its related materials destined for the consumer.

The GDP procedures should include the quality management of personnel, premises, facilities, stock handling/control, disposal of materials/products, vehicles/equipment or transportation/goods in transit, product recall, self inspection and adequate documentary procedures that preserve the safety, traceability and quality of the material or product or cosmetic.

The GDP also requires that materials and products or cosmetics classified as dangerous drugs, scheduled poisons and psychotropic substances, under the Dangerous Drug Act 1952 (Revised 1980), Poisons Act 1952 (Revised 1989), Poisons (Psychotropic Substances) Regulations 1989 and the Control of Drugs and Cosmetics Regulations 1984 (Revised 2006), are stored and distributed in accordance with the requirements of the respective Acts and Regulations.

The full Guidelines on GDP is available on our website at http://www.bpfk.gov.my/

3. *Reminder for Directive 01/2010: Enforcement of Licensing Requirements on the Premises of Local Veterinary Product Manufacturers in Malaysia*

The directive was issued under Regulation 29 of the Control of Drugs and Cosmetics Regualtions 1984 following the 224th DCA committee meeting in 2010.

Licensing requirements on the premises of local veterinary product manufacturers will be enforced effective from **1st January 2012**. Therefore, the NPCB would like to remind registration holders to comply with these requirements.

During this interim period, the registration of veterinary products would only be considered if the manufacturers possess Good Manufacturing Practices (GMP) status for sterile products. As for non-sterile products, registration might be considered for approval even though the manufacturers have not obtained GMP status.

Product registrations will be revoked for manufacturers who fail to meet the requirements after 1st January 2012.

SUMMARY OF PRESS RELEASES

1. *Consumers Cautioned Against The Use of Cosmetic Products Containing Scheduled Poisons*

The public is advised to avoid purchasing and using the following cosmetic products:

No	Name of Products	Notification Number	Scheduled Poison Detected	Notification Holder	Manufacturer
1	BML HB LOTION	NOT090701336K	Tretinion & Hydroquinone	Excellent Combination Sdn Bhd	BML International Inc., Phillipines
2	KRIM MALAM SHANA	NOT090600820K	Tretinion & Hydroquinone	Nabba Trading	A.S.P. International Herbal Soap. Co. Ltd, Thailand
3	NATASYA GOLD KRIM HERBA	NOT091100971K	Tretinion & Hydroquinone	Perwanza Enterprise (M) Sdn Bhd	Bionano Herba Pharma Sdn Bhd, Malaysia
4	BIOTOX WHITENING HYDRO CREAM	NOT07061310KE	Dexamethasone	Dermedex Sdn Bhd	Laboratories D'Armor S.A., France

No	Name of Products	Notification Number	Scheduled Poison Detected	Notification Holder	Manufacturer
5	YOKO WHITENING CREAM	NOT080100330K	Tretinoin	Haresh Enterprise Sdn Bhd	Siam Yoko Co. Ltd., Thailand
6	SUE BEAUTY NIGHT TREATMENT CREAM	NOT080600138K	Tretinoin	Sky Resources Sdn Bhd	Sky Resources Sdn Bhd, Malaysia

Dexamethasone, hydroquinone and/or **tretinoin** are among the scheduled poisons detected in the cosmetic products above. As a result, product notifications of these cosmetics have been cancelled by the Director of Pharmaceutical Services.

The usage of such poisons in cosmetic products are strictly prohibited. Preparations containing these poisons may cause various side effects to consumers.

Anyone who is in possession of these products is advised to immediately stop selling/distributing/using them. Dealers are reminded that the posession of these products is an offence under the Control of Drugs and Cosmetics Regulations 1984.

Scheduled Poisons Detected in Cosmetic Products

- ***Tretinoin*** *can cause skin redness, skin peeling, sunlight sensitivity and discomfort.*
- ***Hydroquinone*** *can cause skin redness, discomfort, skin discoloration, hypersensitivity and a gradual blue-black darkening of the skin. It inhibits the pigmentation process (depigmentation) which attenuates the ability of the skin to protect our body from harmful UV rays and excessive sunlight that increases the risk of skin cancer.*
- ***Dexamethasone*** *is a steroid that (when used topically) can cause skin irritation, dry skin, acne, skin thinning and increased risk of skin infections. Prolonged use of topical steroids may lead to systemic side effects such as suppression of the adrenal glands, metabolic disturbances, impairment of the immune response, etc.*

2. *Shampoo Containing Substance That Is Used in Floor Cleaning Detergents*

An article published in KOSMO Newspaper on 8th March 2011 reported that shampoos are claimed to contain sodium laureth sulfate (SLS) which is a substance normally used in floor cleaning detergents. This substance may cause adverse effects on hormone systems including skin damage.

SLS is commonly used in cosmetic product formulations as cleansing agent, emulsifying, stabiliser and solubiliser. Besides, it is also used as surfactant that acts as a cleaning agent and foaming agent which are widely used in shampoo, shower gel, facial cleanser and toothpaste. This substance is usually used in cosmetic product formulations that involve discontinous and brief use followed by rinsing off the skin. The SLS found in cosmetics is of specific grades intended for the use in cosmetic product formulations.

To date, no report on safety issues has been received regarding the use of SLS in cosmetic products.

SLS has not been listed as a prohibited substance in cosmetic product formulations as no scientific data has indicated that SLS may cause adverse effects if used at the usual concentration level found in cosmetic products. However, there are data showing skin and eye irritation if the substance is used in preparations that do not require rinsing. Therefore, the public is advised to comply to the label regarding the directions for use when using products that contain such substance.

The NPCB will continue monitoring cosmetic products that contain SLS through the Cosmetic Products Quality Control Programme (Program Pengawasan Mutu Produk Kosmetik Bernotifikasi) in order to ensure the safety and quality of these products.

Did You Know?

While there is some argument over the exact origin of shampoo, most believe it can be traced to the Hindi origins of "champo." This refers to a head massage technique that used oils and was found in India in the 1700s. British colonialists took the word and the techniques back to Britain and in the mid-1800s, when shampoo was widely used as a hair treatment. In the 1920s, mass production of bottled shampoo began in Britain and the United States; replacing regular soap in hair cleaning.

DCA NEWS

Summary of the Drug Control Authority (DCA) policies/decisions from January till March 2011:

DCA Meetings	DCA Policies/ Decisions
237th Meeting 17/03/2011	**1. The registration for the two products below have been cancelled due to adulteration:** Product Name: **JCare - su** Registration Number: MAL07090966TC Registration Holder: Usaha Kiara Sdn. Bhd. Manufacturer: Len Fa Medical Supplies (M) Sdn. Bhd. Product Name: **JCare - in** Registration Number: MAL07124653TC Registration Holder: Usaha Kiara Sdn. Bhd. Manufacturer: Len Fa Medical Supplies (M) Sdn. Bhd. The laboratory test results by BPFK showed that the products above contain glibenclamide. Glibenclamide is a controlled medicine for diabetic patients. It can only be supplied by doctors or available at pharmacies upon a prescription. The usage of glibenclamide without proper diagnosis and monitoring by the doctor can cause serious adverse events such as hypoglycemia (excessive reduction in blood sugar). Symptoms of hypoglycaemia include dizziness, tremor, sweating, confusion and lethargy. Severe hypoglycaemia may lead to convulsion, unconsciousness or coma. Hence, these products can cause detrimental effects to consumers who are diabetic and who are at high risk of getting these adverse events. The public is advised to stop using it and they can seek further advice from healthcare professionals, if needed.

UPCOMING EVENTS

1. *International Conference on Harmonisation-Global Cooperation Group (ICH-GCG) ASEAN Training Workshop for ICH Q5C : Stability Testing for Biotechnological/Biological Products*

The NPCB will be organising The ICH-GCG ASEAN Training Workshop for ICH Quality Guideline ICH Q5C: Stability Testing for Biotechnological/Biological Products on 30th-31st May 2011 in Malaysia. This training workshop will provide a great opportunity for upskilling of knowledge and sharing of experiences between regulators and industries from ASEAN countries.

Venue:
One World Hotel
First Avenue, Bandar Utama, 47800 Petaling Jaya, Selangor, Malaysia

Objectives:
- To understand the scientific basis of stability guidelines.
- To update and enhance technical and practical knowledge on stability testing requirements for biotechnological/biological products (ICH Q5C), comparability (ICH Q5E) and specifications (ICH Q6B).
- To better understand how to design, conduct stability studies for biotech products.

The training will focus on:
- Stability studies: protocol, design, specifications etc.
- Relevant quality aspects of stability evaluation.
- Comparability of products subjected to changes in manufacturing process.
- Update on latest regulatory and EU experience on Biosimilars and Advanced Therapy Medicinal Products (ATMPs).

* The registration form and tentative programme schedule are downloadable from our website at http://www.bpfk.gov.my/

Association of Southeast Asian Nations ***The International Conference on Harmonisation***

2. *ASEAN Consultative Committee for Standards and Quality (ACCSQ)*

The ACCSQ was formed by the ASEAN Economic Ministers in 1992 with the aim of removing technical barriers to trades in order to facilitate the implementation of the Common Effective Preferential Tariff (CEPT) Agreement to realize the ASEAN Free Trade Area (AFTA). Two upcoming events of the ACCSQ are:

Events	Organiser	Date	Venue
a) 15th ACCSQ - Traditional Medicine Health Supplement Working Group (TMHS-WG) Meeting	National Pharmaceutical Control Bureau (NPCB), Malaysia	27th June – 1st July 2011	Grand Dorsett Hotel, Subang Jaya, Selangor, Malaysia

Events	Organiser	Date	Venue
b) 18th ACCSQ – Pharmaceutical Product Working Group (PPWG) Meeting	Health Sciences Authority (HSA), Singapore	7th June – 10th June 2011	Grand Copthorne Waterfront Hotel, Singapore

NEW NPCB CLIENT'S CHARTER

1. PRODUCT REGISTRATION **DURATION**

Full Evaluation

- To evaluate application for registration of:
  - o Prescription drugs 210 working days*
  - o Non-prescription drugs 210 working days*
  - o New drugs and biologicals 245 working days*

Abridged Evaluation

- To evalute application for registration of health supplements and traditional products containing:
  - o Single active ingredient 60 working days*
  - o 2 or more active ingredients 80 working days*
  - • Issuance of cosmetic notification 3 working days^
  - • Change of registration holder 45 working days*
  - • Certificate of Pharmaceutical Product (CPP) 15 working days*
  - • Change of manufacturing site 45 working days*

2. LICENSING

- Issuance of manufacturer's, wholesaler's and importer's license 10 working days*
- Evaluation of import license application for Clinical Trial License (CTIL) and Clinical Trial Exemption (CTX):

o For products involving First-in-Man Study, biological products and Advance Therapy Medicinal Product (ATMP) 45 working days*

o For products other than stated above 30 working days*

3. LABORATORY TESTING

- Sample testing for purpose of registration 65 working days#

*Upon receipt of complete application

^For applications fulfilling ASEAN Cosmetic Directive (ACD) requirements

#Upon receipt of sample and complete documentation

CONTACTS & MAP

National Pharmaceutical Control Bureau + 603 - 7883 5400

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
• Variation Section	5588
• Cosmetic Section	5532
Centre for Investigational New Product – Deputy Director	5581
• Investigational Product Evaluation and Safety Monitoring Section	8405
• Research Compliance Section	8401
Centre for Compliance and Licensing – Deputy Diretor	5564
• GMP Section	5566
• Quality, Certification, Licensing and GDP Section	5569
• Clinical Research and Compliance Section	5553
Centre for Organisational Development – Deputy Director	5555
• Information, Communication & Technology Section	5556
• Quality System Section	5429
Centre for Quality Control – Deputy Director	8457
• Bio-Pharmaceutical Testing Section	8448
• Research and Development Section	5462, 5456, 5450
• Pharmaceutical Chemistry Testing Section	5431
• Laboratory Services Unit	5471
• Natural Product Testing Section	5468
• Reference Standard Unit	8458
Centre for Administration – Head	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:

http://www.bpfk.gov.my