Berita
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NEWSLETTER OF THE DRUG CONTROL AUTHORITY MALAYSIA

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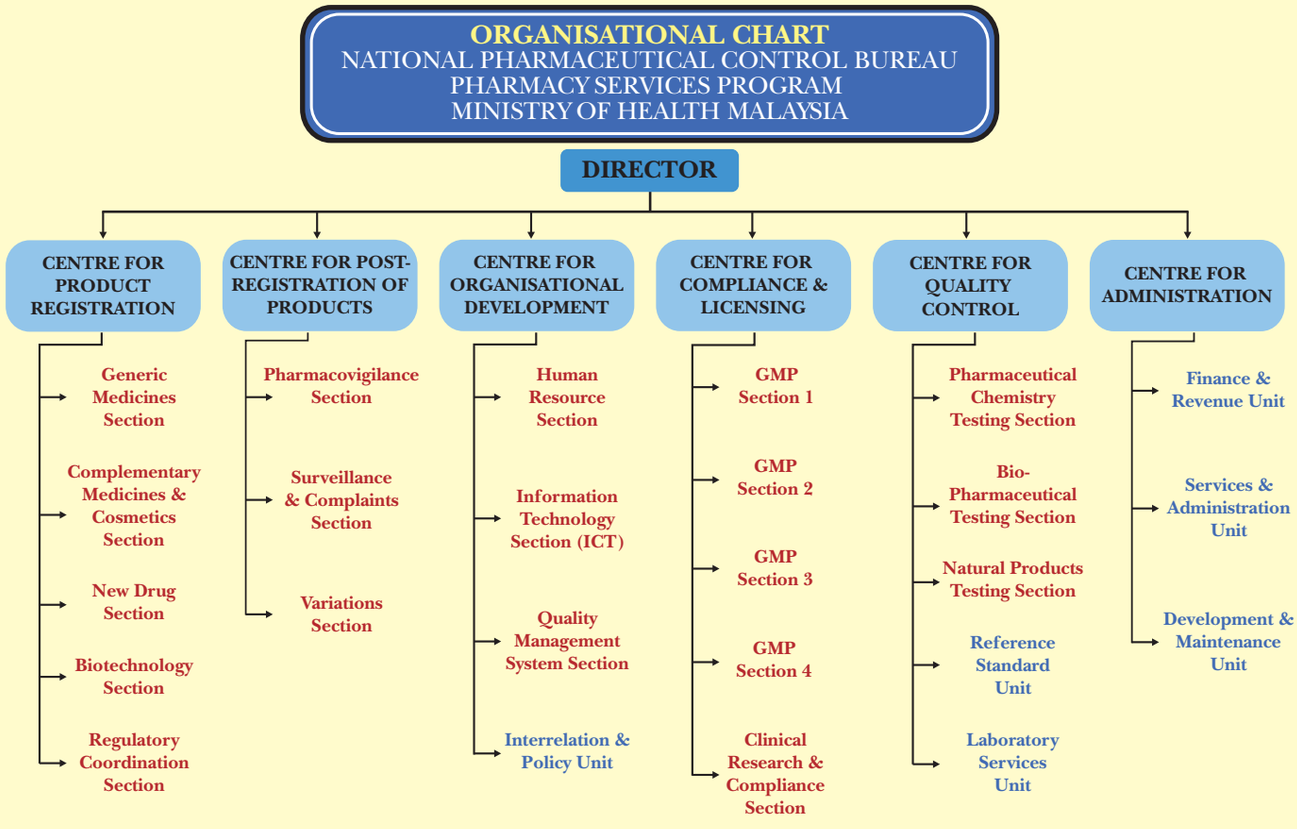


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# IMPLEMENTATION OF REGISTRATION OF VETERINARY PRODUCTS IN MALAYSIA

The Drug Control Authority (DCA), at its 191st meeting held on the 29th March 2007 decided to implement the registration of veterinary products in Malaysia. The implementation date for manufacturers/importers/distributors dealing with veterinary products to submit applications for product registration for all categories of products with the exception of cosmetics shall be announced through the media by the Minister of Health. The implementation date is targeted for the 3rd quarter of 2007.

Applications for the registration of existing veterinary products in the market will have to be submitted within one year from the implementation date.

All veterinary product registration applications must be submitted through a web-based online system via http://www.bpfk.gov.my.

The processing fee for registration of veterinary products shall be similar to the current processing fee and charges for product analysis/analytical evaluation conducted by the laboratory (Centre for Product Quality).

| No. | Product category | | Analytical Evaluation (RM) | Processing Fee (RM) | Total per product (RM) |
|---|---|---|---|---|---|
| 1. | Pharmaceuticals | One active ingredient | 1,200.00 | 1,000.00 | 2,200.00 |
| | | Two or more active ingredients | 2,000.00 | | 3,000.00 |
| 2. | Innovator/New Chemical Entity | One active ingredient | 3,000.00 | 1,000.00 | 4,000.00 |
| | | Two or more active ingredients | 4,000.00 | | 5,000.00 |
| 3. | Herbal Preparations | | 700.00 | 500.00 | 1,200.00 |

The National Pharmaceutical Control Bureau (NPCB) will conduct road-shows and awareness programmes in an effort to assist the industry to better understand the regulatory requirements and steps on how to use the online registration system. Applicants who are not familiar with the on-line registration system are advised to refer to the guidance documents found on the website or to contact the National Pharmaceutical Control Bureau if necessary.

The draft Guidance Document for the registration of veterinary products has been posted on the NPCB's website since March 2007. It has also been distributed to the relevant stakeholders for comments. Feedback received will be taken into consideration and a consensus will be reached before the adoption of the final guideline.

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# DIALOGUE ON THE MALAYSIAN PRINCIPLES OF GOOD LABORATORY PRACTICE (GLP) DRAFT

A dialogue on Malaysian Principles of Good Laboratory Practice was held on the 20th Mac 2007 at the National Pharmaceutical Control Bureau and it was organized by the National GLP Committee, Ministry of Health, Malaysia. The opening session of this dialogue was officiated by Y. Bhg. Tan Sri Datuk Dr. Mohd Ismail Merican, the Director-General of Health, Ministry of Health Malaysia. Representatives from various ministries, government agencies, universities, PhAMA, MOPI and the private sectors attended the dialogue session.

The main aim of this dialogue session was to introduce the Malaysian Guidelines on Good Laboratory Practice Draft. In tandem with Vision 2020 and Malaysia's aspirations to be a developed nation, the pre-requisite international standards and practices must be put in place so that Malaysia is able to compete in the global arena. In the health care sector, it is pertinent that clinical research undertaken as well as medicinal products developed must comply with the accepted global standards. The current guidelines include Good Laboratory Practice (GLP), Good Clinical Laboratory Practice (GCLP), Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP).

The Malaysian Principles of Good Laboratory Practice Draft is based on OECD Principles on Good Laboratory Practice. The draft was indeed the product of close collaboration between the Ministry of Health, Ministry of Science, Technology and Innovation (MOSTI), the academia and the industry organisations namely PhAMA and MOPI. It is hoped that by introducing the Malaysian Principles of Good Laboratory Practice, we will move forward towards enhancing and expanding our research capabilities.

With great emphasis on quality, the GLP compliance programme is a quality system to assist R & D laboratories in adopting systematic processes in planning, performing, monitoring, recording and archiving. Such a system will give customers greater assurance of the integrity of the research data, and also enable us to reconstruct the studies in their entirety from archived data.

The aim of establishing the Principles of Good Laboratory Practice is to promote the development of quality data. Comparable quality of test data forms the basis for mutual acceptance of data among countries. If individual countries can confidently rely on test data developed in other countries, duplicative testing can be avoided, thereby saving time and resources. The application of these principles should help to avoid the creation of technical barriers to trade, and further improve the protection of human health and the environment.

With this issue being timely addressed, we hope that Malaysia will be recognized as a member of the non-OECD country adhering to the Mutual Acceptance Data (MAD) system in the near future, where test data generated in Malaysia will be accepted in all OECD countries.

The Malaysian Principles of Good Laboratory Practice will complement other existing guidelines related to clinical and drug development research such as the Malaysian Good Clinical Practice Guidelines, Guidelines for Application of Clinical Trial Import License and Clinical Trial Exemption in Malaysia; and Guidelines for Research and Development in Herbal Medicines for herbal products.

# CDER FORUM FOR INTERNATIONAL DRUG REGULATORY AUTHORITIES


Two officers from the National Pharmaceutical Control Bureau namely Ms Abida Haq and Ms Saleha Md Ewan were priviliged to attend the U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER) Forum which was held in Rockville, Maryland USA on 16-20 April 2007.

The U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER) holds this forum to give an opportunity to other regulators to learn about its drug review process and also for the exchange of drug regulatory information between the U.S. FDA CDER and its counterpart agencies in other countries.

The CDER Forum was attended by participants from several ASEAN countries i.e. Singapore, Vietnam, Philippines and Indonesia as well as the other regions (Brazil, Pakistan, Ethiopia, Armenia, Japan, Uganda and Korea). The forum served to provide an insight into the work processes as well as the science, technology, regulations used by the FDA in their day to day work.

The scope of the training covered the review processes for New Drugs, Generic Medicines, Over-the-Counter products as well as the specialty reviews involved for biologics and pediatric products. The training also provided in-depth information on the labeling compliance in the US, bioequivalence studies, Good Manufacturing Practices, risk management plans, surveillance activities, drug safety monitoring and the mechanism for the monitoring of advertisements.

Many parallels can be drawn between the regulatory practices in the US and Malaysia but there is also many differences between the two systems. Given the number of highly trained scientists attached to the US FDA, the review process for New Drugs is far more detailed and the FDA is involved from a very early stage during the drug development process itself. It was very interesting to learn the review process for generic medicines and the control mechanism for OTC products.

In the US, OTC products which are already in the monograph can be sold without prior approval from the FDA. Nevertheless they are subjected to the same standards for safety and effectiveness as prescription drugs. Labeling is an integral part of the OTC products and they have to comply with the labeling regulations to ensure that consumers understand the labels in order to use these products safely and effectively. As the NPCB is continually trying to improve the drug registration process, due consideration will be given to what has been observed in the US to study ways and means to streamline and expedite the registration process of low risk products such as the OTCs.

## MALAYSIA'S STAND FOR PROMOTING GENERIC MEDICINES

Realising that the pharmaceutical industry is an integral component of the healthcare sector, a multi-prong approach has been taken to help in the growth and development of the domestic industry which has so far been mainly involved in the manufacture of generic medicines.

As of December 2006, there were 336 pharmaceutical companies licensed by the Drug Control Authority which is the drug regulatory arm of the Malaysian Ministry of Health. Of these, 161 are involved in the production of traditional medicines, 85 pharmaceuticals and 90 cosmetics.

During the period 1996-2005, the industry registered encouraging growth with expansion and diversification into a wider range of generic products and increased exports. The Malaysian pharmaceutical industry has the capability to produce almost all dosage forms, including sterile preparations such as eye preparations, injectibles, soft gelatin capsules and time release medications.

Malaysian pharmaceutical manufacturers are focusing on high-margin niche segments, adding value to existing products through improved drug-delivery technologies, and increasingly moving into biopharmaceuticals and branded generics including biogenerics in order to remain competitive.

Currently, the local industry is producing about 25% - 30% of the domestic demand and has the capability to manufacture more than 80% of the product categories in the National Essential Drugs List of Malaysia. The sales value of locally produced pharmaceuticals has grown at an average annual rate of 10.8% from RM334 million in 1996 to RM852 million in 2005.

Compliance with the international code on Good Manufacturing Practices has been fundamental in improving the standards of local manufacturers. The high quality of locally manufactured generic products has enabled its penetration into the Asia-Pacific Rim countries, the Middle East, Africa and Latin America. With the admission of Malaysia as a member of the Pharmaceutical Inspection Cooperation/Scheme (PIC/S) since January 2002, the country's exports of pharmaceutical products received a boost, especially among the member countries, which include the EU, Australia and Canada. In 1996, exports of pharmaceuticals was valued at RM194 million and it increased to RM494.3 million in 2005.

Malaysia's Intellectual Property laws conform to international standards and provide adequate protection to both local and foreign investors. Total investments in the pharmaceutical industry for the period 1996-2000 amounted to RM95.7 million and this escalated almost ten fold to RM911.2 million during 2001-2005. Sources of foreign investments were Germany, Taiwan, India, UK, Australia, Norway, Singapore and the People's Republic of China.

Currently, the manufacture of pharmaceuticals and related products are eligible for normal Pioneer Status or Investments Tax Allowance incentives. The development, testing and production of pharmaceuticals promoted under biotechnology are eligible for High Technology Pioneer Status or Investments Tax Allowance incentives.

In terms of human resource, the government has facilitated the establishment of pharmacy schools both in the public and private institutions of higher learning in an effort to meet the growing needs of the industry for adequately trained personnel. However, as a short term measure to overcome the shortage of specific skills, immigration laws have been amended to allow the industry to employ foreign skilled personnel on a contract basis.

In the field of R&D, joint collaborations and commercialisation of research projects have been established between the industry, universities and research institutes. Research collaborations have also been established between the government, local universities and Malaysian companies with foreign research institutes to enable technology transfer such as the collaboration with Cuba for the production of vaccines.

The drug regulatory framework has also contributed significantly to the growth of the generic medicines market. With the introduction of the on-line registration system for prescription medicines in mid-2003, the timelines for registration have been expedited through streamlining of work processes. Applications for newly off-patented medicines are accorded priority review and this has allowed for faster entry of these generics in the market.

In an endeavor to improve and ensure the quality and efficacy of generic medicines, requirements for bioequivalence/bioavailability (BE/BA) have been introduced. Currently, BE/BA studies have to be conducted for 69 products. A national BE/BA committee has been established comprising regulators, industry players, academia as well as the BE centres to ensure that workable policies are implemented. The government is also currently looking into ways to further improve the BE centres so that Malaysian generics can have an edge over similar products from elsewhere.

The recently approved National Medicines Policy and the National Health Policy which is being drafted have outlined the need for increased self sufficiency in pharmaceutical supplies, decreased reliance on imports and the promotion of use of generic medicines wherever possible. These policies will further help to spearhead the growth of the generic medicines industry in Malaysia.

Malaysia is a signatory to the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS). In addition to this, Malaysia ratified the Patent Co-operation Treaty (PCT) in 2003, facilitating patent registration and consequently protection to foreign inventions. However, Malaysia was the first Asian country to institute the provisions for compulsory licencing of anti-retroviral drugs in an effort to make treatment more affordable for HIV positive patients.

Although the pharmaceutical industry in Malaysia is highly regulated, the government nevertheless has worked closely with the industry. Dialogues are held on a regular basis, training especially on GMP have been provided and technical working groups comprising regulators and industry representatives have been established to address issues of concern.

The Malaysia – US FTA is in the final stages of negotiations. One of the key issues being addressed is that of Intellectual Property Rights (IPR) and Data Exclusivity (DE) which will have far reaching implications on the generics industry. As accessibility and affordability of drugs is key in any healthcare system, the Malaysian government will endevour to ensure that the health and well being of the nation is not compromised at the expense of trade.

*Paper presented by Abida Haq, National Pharmaceutical Control Bureau, Ministry of Health Malaysia at the Asia Generics Medicines Congress 2007 held in Singapore 27-28 March 2007*

# NEWS & ANNOUNCEMENTS

## Hologram Security Device (Meditag™): Increased Security Features

As provided under Regulation 8(1) of the Control of Drugs and Cosmetics Regulation 1984, the requirement for the affixation of this security device to product labels, is applicable to pharmaceutical products, traditional products and health supplements. The use of the Meditag Security label has been enforced for products regulated by the Drug Control Authority with the exception of cosmetics, external personal care products and products such as vaccines which require special handing since May 2006.

In tandem with the Ministry of Health's effort to further enhance the safety of consumers in using pharmaceutical and traditional products purchased over the counter, starting May 2007, retail pharmacies located in strategic areas in Malaysia will be provided with a scanner which enables the public to detect the authenticity of the security label. This project will be executed in stages.

## Exemptions and Import License for Registration of Homeopathic Products

All homeopathic products shall be registered with the Drug Control Authority (DCA) prior to importations into Malaysia. Currently, the registration for homeopathic products and other natural product categories shares similar registration procedures. The Guidance Document for Homeopathic Medicines is in the drafting stage prior to reference as a formal document. At present, the importations of single remedy homeopathic dilutions and mother tincture are exempted from registration with the DCA. However, these dilutions should not contain any quantities of traceable active ingredients, and it should only be used by homeopathic medicines practitioners for the treatment of patients. Mother tinctures which contain narcotic substances such as cocaine, morphine, opium and such are not allowed to be brought into this country.

## Switzerland as Reference Country

Based on its good cooperation and raport, the DCA at its 191st meeting held on 29 March 2007 agreed to include Switzerland as a reference country for registration evaluation purposes. At present the reference countries for the purpose of product registration include the United States of America, United Kingdom, France, Japan, Australia, Canada and Sweden.

# Warning Statement on Label and Package Insert of Products Containing Glucosamine

The DCA at its 193rd meeting held on 24 May 2007 agreed that the warning statement on label and package insert of products containing glucosamine to be updated.

The following warning statement should be included under 'SIDE EFFECTS' in the package insert:

**CARDIOVASCULAR**
Peripheral oedema, tachycardia were reported in a few patients following larger clinical trials investigating oral administration in osteoarthritis. Causal relationship has not been established.

**CENTRAL NERVOUS SYSTEM**
Drowsiness, headache, insomnia have been observed rarely during therapy(less than 1%)

**GASTROINTESTINAL**
Nausea, vomiting, diarrhea, dyspepsia or epigastric pain, constipation, heartburn and anorexia have been described rarely during oral therapy with glucosamine.

**SKIN**
Skin reactions such as erythema and pruritus have been reported with therapeutic administration of glucosamine.

# Warning Statement on Package Insert of Products Containing Sedatives-Hipnotics

The DCA at its 193rd meeting held on 24 May 2007 agreed that the following warning statement should be included under 'WARNING' and 'PRECAUTIONS' on package insert of products containing sedatives and hypnotics.

- Anaphylaxis ( severe allergic reaction) and angioedema (severe facial swelling) which can occur as early as the first time the product is taken
- Complex sleep- related behaviors which may include sleep driving, making phone calls, preparing and eating food while asleep

List of registered sedative-hypnotic products that must contain this warning statement include:

- Zolpidem tartrate
- Flurazepam hydrochloride
- Triazolam
- Midazolam

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# DCA NEWS

## NEW SAFETY CONCERNS RELATING TO THE USE OF ZELMAC® (TEGASEROD)

Tegaserod is used to relieve pain, bloating, and constipation caused by irritable bowel syndrome (IBS; a condition that causes stomach pain, bloating, constipation, and diarrhea) in women whose main symptom is constipation. This medication is also used to increase the frequency of bowel movements and relieve bloating, straining, and stomach pain in women and men with chronic idiopathic constipation. Tegaserod is a 5-$HT_4$ agonist, in a class of medications called serotonin agonists.The drug functions as a motility stimulant, and achieving its therapeutic effect by the activation of the 5-$HT_4$ receptors in the enteric nervous system in the gastrointestinal tract. It works by improving muscle movement and the peristaltic effect and increasing production of fluid in the bowels, which alledgedly reduces abdominal pain.

The Drug Control Authority (DCA) is issuing this public statement to inform patients and health professionals about new safety concerns relating to Zelmac® (tegaserod maleate). A new safety analysis conducted by the United States Food and Drug Administration (US FDA) on Zelnorm® ( the brand name under which tegaserod is marketed in the US) found a higher incidence of serious adverse cardiovascular events(e.g. angina, heart attack and strokes) in patients treated with Zelnorm® compared to those treated with placebo (sugar pills). Zelnorm® is being taken off the US market.

In Malaysia, Zelmac® is approved for the symptomatic treatment of female patients with abdominal pain and constipation associated with irritable bowel syndrome (IBS).

DCA at its 193rd meeting held on 24 May 2007 announced the following:

- Products containing tegaserod will no longer be registered in Malaysia as its risks outweigh its benefits.
- Cancellation of registration of Zelmac® 6mg Tablet (MAL20021129A) shall take effect immediately.
- Novartis Corporation (M) Sdn. Bhd., registration holder of Zelmac® 6mg Tablet (MAL20021129A ) is given a grace period of 6 months to ensure that all products are removed from the market.
- Novartis may import Zelmac® 6mg Tablet upon request by prescriber on named patient basis when no such alternative drugs are available for use.

# CONTACT

| ORGANISATION | TEL-EXT |
|---|---|
| National Pharmaceutical Control Bureau | 03-7957 3611 |
| Centre for Product Registration | 270 |
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