BERITA UBAT-UBATAN

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"Champix" (Varenicline) For Smoking Cessation

Safety information has been received from the EMEA dated 14th December 2007 for the attention of all healthcare professionals and patients using Champix (Varenicline). The EMEA stressed that an increase in the awareness of possible adverse reactions i.e. "suicidal ideation and suicide attempts" is crucial based on reports that have been received.

The agency has published media statements as well as questions and answers regarding the safety of Champix. This information may be obtained from their website at www.emea.europe.eu. The EMEA is also working closely with Pfizer, the product registration holder of Champix in updating necessary information to the warning section of the package insert.

In Malaysia, the product has been categorized as Group C poison where it can only be dispensed by healthcare professionals and pharmacists. The product package insert states the following:

Special Warnings And Precautions For Use: Effect Of Smoking Cessation

Smoking cessation, with or without pharmacotherapy has been associated with the exacerbation of underlying psychiatric illness (e.g. depression). Care should be taken

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DCA EDITORIAL TEAM

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with patients with a history of psychiatric illness and patients should be advised accordingly.

Depression, rarely including suicidal ideation and suicide attempt, has been reported in patients undergoing a smoking cessation attempt.

Undesirable Effects

Post marketing cases of MI, depression and suicidal ideation have been reported in patients taking varenicline.
The National Pharmaceutical Control Bureau (NPCB) is currently in the process of updating the product information so that this safety issue is made clear to all relevant parties. All healthcare professionals and pharmacists need to ensure that patients are aware of this information before dispensing the medicine. All patients on Champix need to be counseled on the safety issue of the product.

Good Manufacturing Practice for Cosmetic Premises

The ASEAN Harmonised Cosmetic Regulatory Scheme has been implemented in all ASEAN countries since 1st January 2008. In line with this, the notification system was enforced to replace the cosmetic product registration system. There may have been some confusion among product registration holders on the conformance to Good Manufacturing Practice (GMP) for cosmetic manufacturers. The NPCB wishes to clarify this issue to all relevant parties.

The ASEAN Harmonised Cosmetic Regulatory Scheme consists of two main components:

- ✓ ASEAN Mutual Recognition of Product Registration Approvals for Cosmetics (Schedule A)
- ✓ ASEAN Cosmetic Directive – ACD (Schedule B) that needs to be implemented by all ASEAN countries

The important requirements mentioned in the ASEAN Harmonised Cosmetic Regulatory Scheme are as follows:-

a) Article 3 (Technical Documents For Cosmetics) in the agreement on the ASEAN Harmonised Cosmetic Regulatory Scheme states that **member states shall undertake appropriate measures to adopt and implement the following common technical documents which appear as Appendices and Annexes to the ASEAN Cosmetic Directive or the ASEAN Mutual Recognition Arrangement of Product Registration Approvals, as the case may be** :

g) ASEAN Guidelines for Cosmetic Good Manufacturing Practice.

b) Subject to 1 (c) under Article 8 (Product Information) under ACD states that the method of manufacture complying with the Good Manufacturing Practice is laid down in the ASEAN Guidelines for Cosmetic GMP appearing as Appendix VI ; **the person responsible for manufacturing or importation into the market must possess adequate knowledge or experience accordance with the legislation and practice of the Member State which is the place of manufacture or importation.**

Subject (a) and (b) clearly states that the Good Manufacturing Practice requirements for cosmetic premises are still enforced. As such, each premise in Malaysia will be inspected periodically to ensure that all cosmetic manufacturers comply with the ASEAN Guidelines for Cosmetic GMP.

Press Release: PIC/S Committee Meeting, Krakow, Poland

26th-27th May 2008

A joint committee meeting of the Pharmaceutical Inspection Convention (PIC) and the Pharmaceutical Inspection Co-operation Scheme (PIC Scheme) took place in Krakow (Poland) on 26th-27th May 2008 under the chairmanship of Mr. Jacques Morénas (France / French Agency for the Safety of Health Products). All PIC/S Participating Authorities were represented. Representatives from EDQM, EMEA, UNICEF and WHO as well as from Cyprus' Pharmaceutical Services, France's Veterinary Agency and the US Food and Drug Administration also participated in the meeting.

With regard to the PIC/S committee meeting, the following issues were discussed:-

a) Indonesia's National Agency for Food and Drug control (NADFC) applied for membership on 29th April 2008.

b) Assessment and Reassessment of other Authorities

- The membership applications of Cyprus' Pharmaceutical Services (CPS) and France's Veterinary Agency (AFSSA-ANMV) were reviewed.
- The Committee reviewed the assessment report on Thailand's FDA's application.
- On site assessment visits would be carried out for the US Food and Drug Administration (US FDA), Israel and follow up visits to Lithuania.
- Reassessment of the PIC/S membership for Ukraine Ministry of Health.

The Committee also reviewed the report on the successful reassessment of United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) and agreed to close the reassessment.

c) Training for Inspectors: Meeting of the Working Group

- The meeting of the PIC/S Working Group mainly focused on reviewing the mandates and objectives for 2008 of PIC/S Expert Circles.
- The Working Group also reviewed the draft revision of the Guideline for Expert Circles.
- A Drafting Group was created for the development of Annex 3 on radiopharmaceuticals.

d) Exchange of Information

- The Committee reviewed the draft PIC/S Standard Operating Procedures on Team Inspections describing the way to initiate, plan, conduct, report upon and follow-up inspections to be performed jointly by PIC/S Participating Authorities in non-PIC/S countries.
- Members also noted a list of third-country inspections to be performed by PIC/S Participating Authorities in 2008 and beyond.

e) Guidance Documents

- The committee adopted the mandate of the Working Group on Good Distribution Practices (GDP).
- The revised PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments had entered into force on 1st April 2008.

f) Relations with other Organisations

ASEAN

- During the PIC/S-ASEAN forum held in Singapore on the 22nd November 2007, the ASEAN Task Force on GMP decided to take the PIC/S GMP system and the PIC/S Quality System requirements for Pharmaceutical Inspectorates as a benchmark for ASEAN integration in the field of GMP.

- National Pharmaceutical Control Bureau (NPCB) had shared with PIC/S its new draft GMP guide on herbal medicines which is more detailed and stringent than the current PIC/S GMP Guide.

UNICEF

- The Committee discussed the field of the future co-operation with UNICEF and suggested the latter to consider the possibility to either (i) apply for full PIC/S membership or (ii) to negotiate an associated partnership with PIC/S.

Industry Associations

- Due to the positive outcome received from the first PIC/S- Industry Workshop "Systems Approach to Quality Risk Management" held in Singapore, 23rd November 2007, the next joint workshop would take place in Geneva Switzerland on the 13th – 14th November 2008 on the "Manufacture of Sterile Medicinal Products"

2008 PIC/S Seminar – Krakow

The joint meeting of the PIC/S Committee was followed by a Seminar on "Good Distribution Practices as one of the Key Elements for Quality of Medicinal Products" which was held in Krakow (Poland) on 28-30 May 2008.

The PIC/S Seminar was organised by Poland's Main Pharmaceutical Inspectorate (MPI). Around 120 participants from 40 countries attended the seminar including inspectors from a number of non-Member agencies and organisations coming from CIS, Cyprus, EDQM, EMEA, France (Veterinary Agency), Indonesia, Israel, Lithuania, Serbia, South Korea, Taipei, Ukraine, UNICEF, USA and WHO. It was also the first time that a PIC/S Seminar was attended by a representative from Egypt.

The Seminar focused on:
- the legal aspects of GDP inspections (existing and future guidelines);
- the application of risk analysis in GDP inspection planning;
- the definition of most frequent deficiencies in wholesaling and the development of suitable strategies for inspectors;
- the risk of counterfeit products in legal distribution channels;
- the definition of problems in the scope of distribution of APIs.

Finally, the committee confirmed the next meetings would take place in Geneva, Switzerland on 12th – 13th November 2008 and on 5th-6th May 2009.

The Ninth Meeting of The ACCSQ Traditional Medicines And Health Supplements (TMHS) Product Working Group (PWG)

5th-6th June 2008, Petaling Jaya, Malaysia

The 9th Meeting of the ASEAN Consultative Committee for Standards and Quality (ACCSQ) Traditional Medicines and Health Supplements Product Working Group (TMHS PWG) was held from 5th-6th June 2008 in Petaling Jaya, Malaysia.

The Meeting was chaired by Mr Ruslan Aspan, Deputy of Traditional Medicine, Cosmetic and Complementary Product Control, National Agency of Drug and Food Control, Republic of Indonesia and co-chaired by Madam Abida Haq Syed M Haq, Deputy Director, Centre for Product Registration, National Pharmaceutical Control Bureau, Ministry of Health, Malaysia.

The Meeting was attended by delegates from Brunei

Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Philippines, Singapore, Thailand, Vietnam, representatives from the ASEAN Secretariat and the ASEAN Alliance of Health Supplements Associations (AAHSA). Representatives from the Traditional Medicines and Health Supplements industry of ASEAN Member States were also in attendance as observers.

Progress On The Harmonisation Of Identified Technical Requirements - Updates from the ASEAN TMHS Scientific Committee (ATSC)

The Meeting noted the progress made by the ATSC on the following issues:

1. Harmonization of guidelines for minimising the risk of Transmissible Spongiform Encephalopathies (TSE) in TM and HS. The ATSC had finalized the ASEAN Guideline for Minimising the Risk of TSE in TM and HS.

2. Limit of contaminants
   i) heavy metals
   - the limits for lead at 10 ppm and cadmium at 0.3 ppm;
   - the limit of mercury at 0.5 ppm;
   - removal of copper from the list of contaminants;
   - further discussions on the limit for arsenic;
   - to take into consideration the request by Thailand to re-consider the limits for HS

   ii) Pesticide residue
   The Meeting agreed to establish a Task Force with participation from Malaysia (Lead country), Indonesia, Thailand and Vietnam to further discuss the pesticide residue issues.

   iii) Microbial contamination
   TMHS PWG will harmonise the microbial contamination based on the British Pharmacopoeia (BP) categories and parameters and not on specific limits which will be determined by the respective Member States.

3. Restricted additives and excipients
   The Meeting agreed to consider the use of references such as pharmaceutical references and CODEX General Standard for Food Additives to develop the list of the restricted additives and excipients for TM and HS.

4. Negative list of ingredients
   The Meeting agreed that Indonesia as Lead Country will prepare a single negative list taking into consideration banned substances. The Member States were requested to provide their rationale for the banned substances to Indonesia for compilation after which the ATSC will address those substances that carry less commonality in ASEAN.

5. Classification of products at interface
   ATSC should further discuss the classification of the TM and HS and the products at interface.

6. Maximum level of vitamin and minerals
   The Meeting agreed to adopt the WHO Model as the basis for establishing maximum levels of vitamins and minerals in ASEAN.

"Regional and Global Developments in the Health Supplements and Traditional Medicines" aimed at providing a better understanding on models of the TMHS regulation outside ASEAN and recent scientific developments and market trends in TM and HS and provided a forum to benchmark the ASEAN Model with existing models.

Progress on the harmonization of GMP for TMHS – Updates from the TMHS GMP Task Force Meeting

The Meeting considered the recommendations from the Heads of Delegation and agreed to proceed with a common guideline for TMHS which will address the common issues of TM and HS, with separate annexes for issues

specific to TM and HS respectively.

Progress on the harmonization of Product Placement Requirements

The Meeting agreed to revise the risk factors for ingredients as low-risk, medium-risk, high-risk and for claims as low-level, medium-level and high-level. The risk assessment matrix was also revised to be in line with the revised risk factors. It was agreed to use the revised risk assessment matrix as a starting point for harmonisation of product placement requirements and the Meeting agreed that it may be further revised in the future recognizing the complexity of the TM and HS sector.

The Meeting noted that the guidelines below had been previously tasked as follows:

- Guidelines on Labelling - Thailand
- Guidelines on Claims - Philippines / AAHSA
- Guidelines on Negative List of Ingredients - Indonesia / AAHSA
- Guidelines on Restricted Additives and Excipients - Thailand
- Guidelines on Maximum Limits of Vitamins and Minerals - Thailand / AAHSA
- Guidelines on GMP - Malaysia
- Guidelines on Contaminants - Malaysia
- Guidelines for minimising the risk of TSE in TM and HS - Singapore

The Meeting also further identified lead countries for the development of the following set of guidelines to further support the implementation of the ACTR:

- Guidelines on Product Dossier Submission - Malaysia and Singapore
- Guidelines on Non-clinical Requirements - Indonesia / Philippines / AAHSA
- Guidelines on Clinical requirements - Indonesia / Philippines / AAHSA
- Guidelines for Stability Study and Shelf-life (including containers) - Indonesia/AAHSA

Progress On The Harmonization Of Labeling Requirements

The Meeting urged the Member States to reduce their country-specific labeling parameters in support of the harmonization efforts in ASEAN.

Post Marketing Alert System

The Meeting agreed that the PMAS was an important communication tool for sharing of information on defective and unsafe health products in the market and urged all Member States to participate actively in the PMAS.

Technical Assistance And Capacity Building Programmes

The Meeting was informed that the proposed impact assessment approach should focus on the impacts of the harmonisation and integration initiatives of the TMHS sector on the private sector, government, consumers and economy.

ASEAN Alliance of Traditional Medicine Industry

The Meeting was informed that as of now AATMI's membership comprises traditional medicine associations from Indonesia, Philippines, Singapore and Thailand which are the founding members of the association. Malaysia updated the Meeting that there were three national associations for Traditional Medicines and would like to ensure that all three associations are represented in AATMI. In this regard, the Meeting requested Malaysia to liaise with AATMI on the appropriate representation in AATMI.

The Meeting agreed to recognise AATMI as a provisional member of the TMHS PWG to assist in the provision of technical support and input for the harmonisation of the traditional medicine sector. The AATMI, in the meantime, was also urged to ensure that the regional interest is represented in the association.

The delegates expressed their appreciation to STANDARDS MALAYSIA, Ministry of Science, Technology and Innovation and the National Pharmaceutical Control Bureau, Pharmacy Services Division, Ministry of Health, Malaysia, for the warm hospitality extended and the excellent arrangements made for the Meeting. The Meeting thanked the ASEAN Secretariat for the assistance provided.

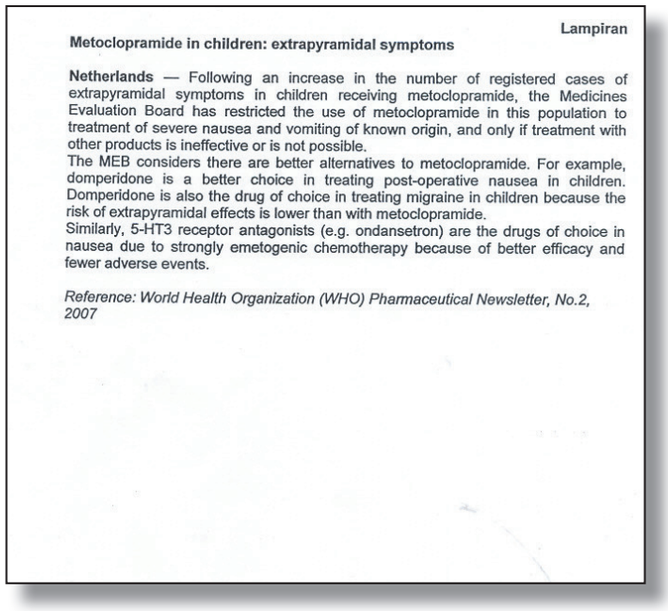
Safety Information Regarding the Use of Metoclopramide in Children

The World Health Organization (WHO) Pharmaceutical Newsletter, No. 2, 2007 has reported that The Netherlands Medicines Evaluation Board (MEB) has decided to limit the usage of metoclopramide in children. This is due to the increase in extrapyramidal symptoms in children who were administered with this drug. MEB has also suggested limiting the usage of this drug for the treatment of 'severe nausea and vomiting of known origin, and only if the treatment with other products is ineffective or not possible'. Alternatives such as domperidone and 5-HT3 receptor antagonist are encouraged as side effects are minimal with these drugs.

Although this matter has been informed to all medical practitioners in Malaysia, the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) is still receiving reports of such adverse effects in children. Therefore, all medical practitioners are reminded to limit the administration of metoclopramide to children to avoid the risk of experiencing extrapyramidal symptoms.

In Malaysia, MADRAC has received 33 reports of extrapyramidal effects experienced in children. Among the adverse effects reported are 'oculogyric crisis (22), spasm (2), neck stiffness (1), jerky movement (1), muscle stiffness (1), eyes gaze upward / eyes rolling (5), speech disorder (1) and back stiffness (1).

MADRAC is continuing its efforts in monitoring the safety aspects of metoclopramide in children and if the drug is found to have more harmful than beneficial effects, specific warnings must be included to the product label. As such, the MADRAC is urging the cooperation of all medical practitioners and pharmacists to monitor the occurrence of these side effects in children and to report these occurrences to MADRAC for further action.



Lampiran

Metoclopramide in children: extrapyramidal symptoms

Netherlands — Following an increase in the number of registered cases of extrapyramidal symptoms in children receiving metoclopramide, the Medicines Evaluation Board has restricted the use of metoclopramide in this population to treatment of severe nausea and vomiting of known origin, and only if treatment with other products is ineffective or is not possible.
The MEB considers there are better alternatives to metoclopramide. For example, domperidone is a better choice in treating post-operative nausea in children. Domperidone is also the drug of choice in treating migraine in children because the risk of extrapyramidal effects is lower than with metoclopramide.
Similarly, 5-HT3 receptor antagonists (e.g. ondansetron) are the drugs of choice in nausea due to strongly emetogenic chemotherapy because of better efficacy and fewer adverse events.

Reference: World Health Organization (WHO) Pharmaceutical Newsletter, No.2, 2007

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Reference: World Health Organization (WHO) Pharmaceutical Newsletter, No. 2,2007

R & D Abstracts

A RETROSPECTIVE STUDY ON THE COMPLIANCE OF PHARMACEUTICAL MANUFACTURERS (POISON PRODUCT) TOWARDS GMP.

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Abstract
Good Manufacturing Practice (GMP) is that part of Quality Assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use. In accordance to the PIC/S (Pharmaceutical Inspection Co-operation Scheme) GMP Guide, there are 9 chapters that form the fundamentals of GMP namely Quality Management, Personnel, Premise/Equipment, Documentation, Production, Quality Control, Contract Manufacture/Analysis, Complaint/ Recall and Internal Audit. GMP compliance is assessed based on deficiencies noted during inspection with regard to chapters as stated in the PIC/s GMP Guide. Deficiencies are classified into critical, major and minor. This retrospective study was conducted to determine the number of reported critical as well as major deficiencies and to identify chapters that mainly contribute to those deficiencies. However, non-routine inspections, minor deficiencies and those from the chapter Quality Management and Quality Control were excluded in this study. Data were extracted from reports of routine GMP inspections which were conducted on pharmaceutical manufacturers (poison products) throughout the year 2006 – 2007. A total of 45 inspection reports were evaluated and 127 critical and 407 major deficiencies were reportedly found in those 45 inspection reports. 61% of critical deficiencies were contributed under the chapter Production whereas 49% of major deficiencies fall under the chapter Premise/Equipment. Despite the critical and major deficiencies that were highly reported under the chapter Premise / Equipment and Production, all of the above-mentioned chapters were inter-related in ensuring GMP compliance. Further study should be initiated to determine ways to increase manufacturer's compliance towards GMP to ensure quality, safety and efficacy of poison products.

Keywords: PIC/s GMP Guide, 9 chapters, GMP, Compliance

ACUTE TOXICITY STUDY (DETERMINATION OF MEDIAN LETHAL DOSE) OF SYNTHESIZED ISONIAZID DERIVATIVE.

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Abstract
Isoniazid is extremely potent with low minimum inhibition concentration (MIC) on Mycobacterium Tuberculosis. Even though it is a drug of choice, error in dosage or intentional overdose may result in life-threatening toxicity. Therefore search for new drugs including isoniazid derivatives with extended spectrum activities and greater safety margin is very important. In this study, 1-isonicotinyl -2-tetradecanoyl hydrazine (INH-C14) derivative of isoniazid was used to compare to isoniazid. 1-isonicotinyl -2-tetradecanoyl hydrazine was gradually administered (orally) to several groups of sprangue-dawley rats. Four groups of 6 male and 6 female rats were selected as treatment group and 1 group of 6 male and 6 female rats were used as the control group. Median lethal dose (LD50) cannot be determined in this study because no group showed 50% death of the rat. The male group showed no significance in weight comparison of internal organs within treatment groups and between treatment group and control ($P<0.05$). The weight of rat also did not show any significant difference within treatment groups and between treatment group and control. The female group showed significant results in comparisons for organ weight within groups for full gut , empty gut, thymus, spleen, right and left kidney ($P<0.05$). In comparing control group and treatment group, significant

results were found for doses of 1200mg/kg and 2400mg/kg for full gut. It was also noted that significant results were seen for groups with dose of 2400mg/kg for empty gut, spleen, left and right kidney. The female group also showed significant difference of body weight in comparison between control and treatment group for administration of dose at 2400mg/kg ($P<0.05$).

Keywords: 1-isonicotinyl -2-tetradecanoyl hydrazine, isoniazid, minimum inhibitory concentration, median lethal dose

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AN EVALUATION ON ERRORS FREQUENTLY OCCURRED DURING EVALUATION OF PRODUCT REGISTRATION VIA QUEST 2 SYSTEM

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Abstract
QUEST 2 is an online system for product registration. Evaluation of registration errors and frequency of error occurrence in each product groups found in the QUEST 2 product registration system is to identify unfamiliar elements among industry players. A retrospective, descriptive study was done by evaluating application forms received during the month of August, 2007 from randomly selected officers of various units in the Centre for Product Registration (PPP). Information on errors was classed into specific categories according to product groups. Element in the evaluation that was being justified as 'No' by evaluators will be considered as an error. A total of 2128 evaluations were taken in for this study involving poison products, over-the-counter products (OTC), traditional products, health supplements and cosmetic products. All were found to have at least one error. For 25 evaluations involving poison products, error was mostly found in 'animal origin' category which fetched a 93% frequency of occurrence. For both 22 OTC and 42 traditional product evaluations, the element with the highest frequency of error occurrence was for 'Label for immediate container' category with 64% and 98%, respectively. As for 13 health supplement applications received, both 'batch manufacturing formula' and 'label for immediate container' categories had the highest frequencies of error occurrence (92%). Of all 2026 cosmetic product evaluations the highest frequency of occurrence was found on 'name of substance' (28%). Identification of these errors and their frequencies of occurrence enable National Pharmaceutical Control Bureau to generate appropriate strategies to enhance understanding among the public and industry players on Quest 2 product registration.

Keywords: Quest 2 system, product registration, poison, over-the-counter, health supplement, cosmetic, traditional

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MANUAL & ONLINE PRODUCT REGISTRATION SYSTEM OF NATIONAL PHARMACEUTICAL CONTROL BUREAU (NPCB) - A TIMELINE COMPARISON

Chin F. F., Pua A.N., Tan T. K., Kok C. F., Mazlifah M.F., Zakiah A.G.,
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Abstract
NPCB has upgraded the product registration system from the manual to online system since 2003, aiming to improve the timeline of product registration processes. The objective of this study is to compare the timeline between online and manual product registration system; to investigate the contributing factors of delay in product approval. A randomized retrospective study was done on manually registered products from January till March 2003 and online products from October till December 2007. A prospective evaluator comparative satisfaction survey between online and manual product registration procedure of Centre for Product Registration was also included in the study. The study included Non-Prescription, Prescription and Natural Products and excluded 'For Export Only" products. The survey was done by excluding evaluators who only have done online registration. There were 406 products registered through

manual submission by the Drug Control Authority (DCA) 143-145, and 271 products were registered through online submission by the DCA 198-200. Online registration timeline for Non-Prescription, Prescription and Natural Product presented mean values of 12.7, 8.4 and 7.7 months respectively as compared to manual registration which presented mean values of 25, 30.7 and 16.6 months respectively for each category of product; these showed 49.6%, 40% and 41.8% of timeline improvement respectively. For prospective evaluator-satisfaction survey, the overall finding showed that most evaluators preferred online product registration system to the manual system. Online registration system is able to improve timeline of product approval process. Communication problem between applicant and evaluator, and incomplete data from applicant are the major factors that contribute to the delayed timeline of product approval.

Keywords: online, manual, timeline, product registration system, product

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A SURVEY ON AWARENESS AND KNOWLEDGE OF BIOTECHNOLOGY AND BIOSIMILAR PRODUCTS AND THEIR REGISTRATION AMONG APPLICANTS.

Vidhya H, Suzana M.N, Zahura M, Arpah A
Biotechnology Section, Centre for Product Registration,National Pharmaceutical Control Bureau (NPCB).

Abstract
Biopharmaceuticals are highly complex proteins produced by recombinant technology. Due to their inherent complexity and sophisticated manufacturing processes, it is virtually impossible to produce identical copies of the originator product. Thus, biosimilars or follow-on products of established biopharmaceuticals cannot be termed as biogenerics. Delivering a biosimilar product of quality, safety and efficacy to a patient involves complex technical and regulatory challenges. This study was conducted to evaluate the knowledge regarding biotechnology and biosimilar products among applicants, to assess the awareness on regulatory perspectives and to identify areas of improvement and training pertaining to biopharmaceuticals. This was a descriptive survey using a convenient sampling method in February 2008. The self-administered questionnaire which contained 3 sections assessing concepts, awareness and knowledge was distributed prior to commencement of a NPCB workshop and by other means to applicants from pharmaceutical companies (regulatory). Out of 100 questionnaires, 77% responded. Results showed a good understanding of concepts in biotechnology and biosimilar products in 76.8% respondents. Lack of awareness was identified in concepts of comparability studies (42.9%), International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals (ICH) guidelines (45.5%) and Malaysian regulatory requirements for biosimilars (42.9%). 45.5% applicants said that biogeneric is not a biosimilar while 37.7% felt biosimilars will bring cost-saving to healthcare. Majority agreed that clinical studies (58.4%) and pharmacovigilance (49.4%) are needed for biosimilars and that regulatory process of biosimilars is still evolving worldwide (58.4%). This study demonstrated good understanding of basic concepts. However, a need remains to increase awareness and knowledge of biopharmaceutical guidelines and the Malaysian regulatory requirements of biosimilars among applicants.

Keywords: Biotechnology, Biopharmaceuticals, Biosimilars, Knowledge, Awareness, Regulatory

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A RETROSPECTIVE STUDY ON THE TREND OF REGISTRATION OF SELECTIVE ACTIVE INGREDIENT FOR PHARMACEUTICAL HEALTH SUPPLEMENT IN MALAYSIA FROM 2002-2007

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National Pharmaceutical Control Bureau

Abstract
In Malaysia, registration of health supplement products started in the year 1988. Health supplement products are solid dosage forms,

liquids or powders product/s taken orally and are intended to supplement the diet. They are not represented as a conventional food or as a sole item of a meal/diet. The aim of the study was to describe the trend of registration of different classes of active ingredient(s) in registered pharmaceutical health supplement products from 2002-2007. It was also aimed to compare between the different classes of active ingredient(s) of health supplement registered. This was a retrospective study and only selected pharmaceutical health supplement were studied such as multivitamins, flavonoids, caretenoids, oil, probiotics, amino acids, and enzymes. The frequency of each class of active ingredient was obtained from the Quest 2 database. For products containing two or more classes of active ingredients, the product was included in all three classes. Products that contain 2 or more vitamins were considered as multivitamins. The data were analyzed using Microsoft Excel 1997 and a descriptive analysis was carried out. From 2002-2005 there was an increase in the frequency for each class of active ingredient registered. From 2005-2006 , the trend demonstrated a sharp increase of 161%, 172%, 111%, 163%, 100%,138% and 100% for multivitamins, flavonoids, carotenoids, oil, probiotics, amino acids and enzymes. However, there was a decrease in frequency of registered active ingredients for all of the selected classes in 2007. As a conclusion, the trend for all classes of active ingredients demonstrated a similar pattern which was a gradual increase from 2002-2005, a sharp increase from 2005-2006 and a decrease from 2006-2007.

Keywords: Trend, Frequency, Registration, Active ingredients, Health Supplement

SCREENING OF HYDROQUINONE IN COSMETICS PRODUCTS BY THE QUALITY CONTROL CENTRE IN 2006 AND 2007

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National Pharmaceutical Control Bureau, Ministry of Health Malaysia

Abstract
In Malaysia, hydroquinone is classified as a scheduled poison and is not allowed to be used as an ingredient in cosmetic products. However, it has been used to adulterate cosmetics as it is an effective skin whitening agent. The National Pharmaceutical Control Bureau (NPCB) is actively monitoring cosmetic products marketed in Malaysia through surveillance activities to ensure that products are safe, of quality and free from adulteration. The objectives of this study are to screen the presence of hydroquinone in cosmetic products available in the market and to make an assessment from the data extracted. Retrospective data was extracted and analyzed from NPCB's database (Quest 2) for cosmetic samples screened in the year 2006 and 2007. Detection was done by using Gas Chromatography Mass Spectroscopy (GCMS). A total of 321 samples were tested which include both local and imported products. From the data, 283 (88.2%) were market-surveillance samples and 38 (11.8%) were enforcement samples. Hydroquinone was detected in 38 samples (11.8%) and 13 samples were found to contain both hydroquinone and tretinoin. Out of 38 positive samples, 13 were enforcement samples and the balance were surveillance samples. In conclusion, the number of samples detected with hydroquinone is small as compared to the total number screened. Sample selection may play an important role in order to get results that will reflect the real number of cosmetics containing hydroquinone in our market. Punitive action was taken for samples detected with hydroquinone.

Keywords : Hydroquinone, Cosmetic, Tretinoin, Surveillance, Screening

SPONTANEOUS REPORTS OF DRUG-INDUCED STEVENS JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS REPORTED TO MALAYSIAN ADVERSE DRUG REACTIONS ADVISORY COMMITTEE (MADRAC) IN MALAYSIA 2000-2007

Y. C. Ong, F. A. Rashid, L. S. Tan
National Pharmaceutical Control Bureau

Abstract
Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are serious and life threatening hypersensitivity events related to the skin and mucous membranes. In Malaysia, there have been many cases of adverse drug reaction reports related to SJS and TEN. The objective of this study is to evaluate the number of adverse drug reaction reports received in Malaysia related to SJS and TEN from year 2000 to 2007 and to evaluate common drugs which cause SJS and TEN. A retrospective study was done based on the Quest 2 database of the National Pharmaceutical Control Bureau. All adverse drug reactions related to SJS and TEN were extracted and analysed. There were 473 reports received on SJS (2000; 4.92%, 2001; 4.19%, 2002; 4.60%, 2003; 3.76%, 2004; 3.90%, 2005; 3.43%, 2006; 3.85%, 2007; 0.95%) and 67 for TEN (2000; 0.38%, 2001; 0.25%, 2002; 0.2%, 2003; 0.38%, 2004; 0.12%, 2005; 0.76%, 2006; 0.28%, 2007; 0.95%) during year 2000 to 2007. Allopurinol and Carbamazepine were found to be the drugs most reported to causing SJS (15.6%, 15.8%) and TEN (17.9%, 14.9%). Due to the seriousness of these adverse drug reactions, MADRAC has decided to advise all healthcare professionals to prescribe these drugs rationally and to counsel patients on adverse drug reactions particularly involving the skin.

Keywords: Stevens Johnson Syndrome, Toxic Epidermal Necrolysis, adverse drug reaction

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SERIOUS SKIN REACTIONS DUE TO SELECTIVE CYCLOOXYGENASE-2 INHIBITORS: EXPERIENCE OF MALAYSIAN ADVERSE DRUG REACTIONS ADVISORY COMMITTEE (MADRAC)

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At present, there are only three Cyclooxygenase-2 (COX-2) selective Non-steroidal Anti-inflammatory Drugs (NSAIDs) registered in Malaysia i.e. celecoxib, etoricoxib and parecoxib. Our objectives were to identify the most adverse drug reactions (ADR) reported based on System Organ Class (SOC); investigate the prevalence, identify and describe the serious skin reactions related to registered COX-2 selective reported to the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC). A cross-sectional, restrospective study design of ADR reports data for celecoxib, etoricoxib and parecoxib was conducted. Data were extracted from Quest2 database and analysed for the year 2006 till 2007. ADR terms, SOC, Erythema Multiforme (EM) (high level term) including symptoms associated with EM for celecoxib, etoricoxib and parecoxib were identified from the database. The total number of ADR terms reported for these NSAIDs was 176. The most frequently reported ADRs were related to skin and appendages disorders, 33.5% followed by gastro-intestinal system disorders, 22.2% and body as a whole-general disorders, 16.5%. Out of 43 suspected cases of celecoxib causing ADR, three cases (7%) associated to EM while two out of nine parecoxib cases (22.2%) related to EM. However, of 46 cases, there was only one suspected report of etoricoxib causing EM associated symptoms (2.2%). In total, there were five reported cases identified causing EM and associated symptoms where two cases of suspected celecoxib; one case due to parecoxib; one case due to etoricoxib while the other one case is due to a combination of celecoxib and parecoxib. These case incidences reported to MADRAC provide useful tools in monitoring, providing information and creating awareness among the healthcare professionals as well as the public on serious skin reactions associated with COX-2 selective products

Keywords: Cyclooxygenase-2 selective Non-steroidal Anti-inflammatory Drugs, Erythema Multiforme, adverse drug reaction.

STANDARDISATION OF COLOUR AND FLAVOUR FOR REGISTERED PRODUCTS CONTAINING METHADONE

The Drug Control Authority (DCA) at its 203rd meeting held on 27th March 2008 decided that the colour and flavour of all registered products containing methadone should be standardised.

PATIENT PACK SIZE FOR PHARMACEUTICAL PRODUCTS

The Drug Control Authority (DCA) at its 204th meeting held on 29th April 2008 decided that appeals on the recently implemented regulation on patient pack size will be considered on a 'case to case' basis, provided that reason(s) given in the appeal is/are acceptable and justified.

EXEMPTION OF BIOEQUIVALENCE STUDY FOR EXPORT-ONLY GENERIC PRODUCTS

The Drug Control Authority at its 205th Meeting held on the 29th May 2008 agreed to grant exemption of bioequivalence studies for locally manufactured generic products that are registered for export-only purposes.

However, product registration holders must present a letter from the relevant authorities of the importing country confirming that bioequivalence study is not a requirement and therefore not necessary. The letter must be submitted together with the application for registration of the said product.

SIX MONTHS DEADLINE FOR SUBMITTING ADDITIONAL/ SUPPORTING DATA

The Drug Control Authority (DCA) at its 205th Meeting held on the 29th May 2008 decided on the above.

The Drug Control Authority (DCA) has decided to reject applications if insufficient/ incomplete data is provided to enable the evaluation of dossiers. Applicants are given 2 reminders within a six month time frame to revert to NPCB and provide the necessary information to complete their registration dossier, failing which , will result in the rejection of the application for registration. The above policy is implemented as follows :

- Applicants are given 90 days from the date of request, to respond and present relevant documents or information.

- The first reminder will be issued if the applicant fails to respond within the stipulated period as above or if the information provided does not assist the evaluation process.
- A second reminder will be issued 60 days after the issuance of the first reminder if the status of the application remains unchanged.

- Subsequent to this, if the NPCB still has not received any response after an additional period of 30 days or the response received is unsatisfactory, the application will be tabled for rejection at the following DCA meeting .

- The policy also covers registration samples that are requested by the Centre for Quality Control, NPCB for testing purposes. Should the applicants fail to submit the samples within 6 months from the date of payment verification, the registration application will be tabled to the DCA meeting for rejection without any reminder being issued.

The above policy is effective as of 29th May 2008 and is applicable to all new applications as well as those that are currently undergoing evaluation process.

NATIONAL REGULATORY CONFERENCE 2008

25th -27th AUGUST 2008

SHERATON SUBANG HOTEL, PETALING JAYA, SELANGOR, MALAYSIA

Organised by:

National Pharmaceutical Control Bureau
Ministry of Health Malaysia

In Collaboration with

Pharmaceutical Association of Malaysia (PhAMA)
Malaysian Organisation of Pharmaceutical Industries (MOPI)
Malaysian Pharmaceutical Society (MPS)
Chinese Medicine Manufacturers Association of Malaysia (PPUCM)
Traditional Malay Medicine Manufacturers Association (PURBATAMA)
Malaysian Dietary Supplement Association (MADSA)
Malaysian Biotechnology Corporation Sdn Bhd (BIOTECHCORP)

Objectives:

- **To disseminate information on new developments and regulatory issues pertaining to pharmaceuticals and complementary medicines**
- **To strengthen the cooperation and understanding between regulators and the pharmaceuticals and complementary medicines industries**
- **To increase the competitive capabilities of pharmaceuticals and complementary medicines industries in line with global trade developments**

Who should attend:

This conference is aimed to benefit Regulators, Industry Representatives (Pharmaceuticals & Complementary Medicines Industries), Researchers and Academia

Registration Fee per participant : RM 1200 (local participants)
USD 500 (foreign participants)

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ORGANISATION	TEL-EXT
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Centre for Product Registration	5457
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Section 2 Complementary Medicine & Cosmetics Section	5522
Section 3 New Drug Section	5514
Section 4 Biotechnology Section	5518
Section 5 Regulatory Coordination Section	5502
Centre for Post Registration	5538
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(i) Reference Standard Unit	5468
(ii) Laboratory Services Unit	5431
(iii) Pharmaceutical Chemistry Testing Section	5450, 5456, 5462
(iv) Bio-Pharmaceutical Testing Section	5442, 5446
(v) Natural Product Testing Section	5471
Administrative Centre	5412

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