WHO ANNUAL REPORT 2003

1. NAME OF COLLABORATING CENTRE

WHO Collaborating Centre for Regulatory Control of Pharmaceuticals

2. ADDRESS

National Pharmaceutical Control Bureau
Ministry of Health
Jalan Universiti
P.O. Box 319
46730 Petaling Jaya
Selangor
MALAYSIA

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3. TERMS OF REFERENCE

The National Pharmaceutical Control Bureau (NPCB) was redesignated as the WHO Centre for Regulatory Control of Pharmaceuticals for a further period of four years from 1 August 2003 to 31 July 2007. The collaborating centre will continue to perform the existing terms of reference which are as follows:-

3.1 To act as a reference centre and support for matters pertaining to pharmaceutical quality assurance and regulatory affairs.

3.2 To continue to collaborate in the current on-going collaborating project among quality control laboratories of ASEAN countries to produce pharmaceutical reference standards.

3.3 To provide training in all aspects of pharmaceutical quality assurance programme

3.4 To carry out product analysis for reference purposes or on behalf of countries lacking quality control laboratories.

3.5 To establish a co-ordinating network for monitoring regulatory matters pertaining to product recall, product defects and other related matters.

3.6 To provide training on computerisation on handling drug regulatory matters.

In addition to this, it was recommended and agreed upon between WHO and NPCB, that the following activities be added to the Centre's terms of reference:

3.7 Closer collaboration with WHO in drug regulatory matters, especially in the field of inspections

3.8 Providing support for training and capacity building of other regional national Drug Regulatory Authorities

3.9 Collaboration in the evaluation of dossiers received from manufacturers expressing interest in the supply of drugs for the treatment of HIV/AIDS, malaria and tuberculosis

4. STAFF LIST

Head of Centre
Hj. Normal bin Sharif - B. Pharm (Hons), M.Sc

Deputy Head
Datin Hasiah bt Hj. Abdullah - B. Sc (Pharmacy)
Eisah bt. Abd. Rahman - B. Pharm, M. Sc., Dip. Medical Microbiology

Officers
The centre has a total of seventy pharmacists

Other supporting staff
Pharmacy assistants - 63
Attendants and general workers - 7
Clerical and administrative staff - 26

5. ACTIVITIES OF THE COLLABORATING CENTRE

5.1 Achievements

5.1.1 Quality Management System

NPCB was successful in upgrading its Quality Management System and was awarded the ISO 9000 version 2000 certification. The scope of the certification was for the regulatory control of pharmaceuticals and traditional medicines through registration, licensing and surveillance activities.

5.1.2 Computerisation

NPCB successfully launched a new computerised system (QUEST 2) which allows for on-line submission of applications for the registration of cosmetics and generic pharmaceutical products which commenced from 1st February 2002 and 1st July 2003 respectively.

5.1.3 Mutual Recognition Agreement

Malaysia was involved in the official signing of the ASEAN Cosmetic Regulatory Scheme Mutual Recognition Agreement, 2 September 2003, Phnom Penh, Cambodia.

5.2 Highlights of projects and activities

5.2.1 7th ASEAN Consultative Committee Meeting

Malaysia hosted the 7th ASEAN Consultative Committee on Standards and Quality (ACCSQ) Pharmaceutical Product Working Group (PPWG) meeting from 1st till 3rd July 2003. The meeting was represented by delegates and observers from Brunei Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Philippines, Singapore, Thailand and Viet Nam. This meeting was preceded by a one-day Validation Seminar, held in Penang, Malaysia, on 30 June 2003. The seminar was co-organised with IFPMA and was well attended by ASEAN participants.

5.2.2 International Course on Regulatory Drug Evaluation

Malaysia co-organised with WHO an International Course on Regulatory Drug Evaluation from 28th July till 1st August 2003 at the NPCB. Twenty participants from Indonesia, Malaysia, Philippines, Singapore and Thailand attended the workshop. The course, which was funded and facilitated by the WHO, offered elements for a standardized evaluation of new drugs that takes into account the specific national situation and therapeutic needs.

5.2.3 Review of WHO Manual

Concurrent with the above-mentioned International Course on Regulatory Drug Evaluation, another meeting co-organised and facilitated with WHO to review the existing WHO Manual on "***Marketing Authorisation of Pharmaceutical Product with Special Reference to Multisource (Generic Product)***" was held on 30th till 31st July 2003. The five ASEAN member countries namely Indonesia, Malaysia, Philippines, Singapore and Thailand sent one participant each. Several pertinent recommendations were put forward by the group for consideration.

5.2.4 Analytical Method Validation Data Workshop

A workshop on Evaluation of Analytical Method Validation Data was conducted in NPCB for the local pharmaceutical industry as well as regulatory officers from 6th till 8th October 2003. The training session was jointly organized with the local pharmaceutical industry organization and was facilitated by a representative from the Therapeutic Goods Administration, Australia

5.2.5 Review of Guidelines for the Registration of Traditional Medicines

A review of Traditional Medicine Registration Requirements was held with representation from the regulatory agency, industry, academia and the pharmacy enforcement division.

5.2.6 Good Clinical Practice (GCP) Audits Training

The centre organised a training session on Good Clinical Practice (GCP) Audits which was facilitated by a representative from the US FDA held on 2 – 4 September 2003 at the NPCB for health professionals, regulators and the industry.

5.3 Consultancies and Representations

Officers from NPCB participated/represented the centre/Malaysia at the following international forums:

- 7th Meeting of ACCSQ- PWG on Cosmetic Manila, Philippines
  (Mrs Anis Talib)

- 7th Meeting of ACCSQ- PWG on Pharmaceutical, Penang
  (several NPCB officers)

- 8th Meeting of ACCSQ-PWG on Cosmetics & 1st ACC Meeting, Hanoi, Vietnam
  (Mrs Anis Talib, Dr Tajuddin Akasah)

- WHO consultation on Good Agricultural and Field Collection Practice for Medicinal Plants, 7 – 9 July 2003, WHO Headquarters Geneva
  (Mr Jaafar Lassa)

- WHO Working Group Meeting on Safety Assessment of Herbal Medicines, 10 – 11 July 2002, WHO Headquarters Geneva
  (Mr Jaafar Lassa)

- Co-Writers Meeting on Quality Assurance for Low Income Countries, 28 Jan – 1 Feb 2003, Maryland, USA and 28 – 30 July 2003, Bangkok, Thailand
  (Mrs Eishah Abdul Rahman)

- WHO Consultation Meeting on Improving Access to Essential Medicines in the Western Pacific Region organized by WHO, 15 – 17 July 2003, Penang, Malaysia
  (Mr. Ramli Zainal)

- A GMP auditor was invited to participate in a PIC/S joint assessment to review the GMP and licensing system in Greece, 12- 19 September 2003.
  (Ms Kadariah Mohd Ali)

- WHO short-term consultants to conduct an assessment of Nepal's regulatory system in aspects pertaining to GMP and GLP requirement for three weeks in December 2003.
  (Mr Lukmani Ibrahim & Mr Jaafar Lassa)

- WHO temporary advisor at the "Expert Meeting On Specification For Pharmaceutical Preparations" in Geneva, 10-14 Mach 2003.
  (Dr Sulaikah Mohideen)

- Review of the draft guidelines entitled "WHO Guidelines on Safety Monitoring and Pharmacovigilance of Herbal Medicines"
  (Mrs Abida Haq)

- 2003 PIC/S Annual Seminar on the Inspection of Quality Control Laboratories, 3 – 6 June 2003, Bratislava, Slovak Republic
  (Mr. Lukmani Ibrahim, Mrs. Faridah Abd. Malek, Dr. Tajuddin Akasah)

- Cosmetic Product Working Group - ASEAN Consultative Committee for Standards and Quality (ACCSQ), 26 – 27 June 2003, Manila, Philippines.
  (Mrs. Anis Talib)

- (SOM III) APEC Life Sciences Innovation Forum, 14 – 15 August 2003, Phuket, Thailand.
  (Mrs Eishah Abdul Rahman)

- Annual PIC/S Blood Circle Meeting, September 2003, Budapest, Hungary
  (Mrs Arpah Abbas)

- 2nd Thailand International Seminar on ASEAN Harmonisation : From Development to Evaluation – Marketing Authorisation, 8 – 10 September 2003, Bangkok, Thailand.
  (Ms Fudziah Ariffin, Mrs Noorizam Ibrahim, Ms Tan Lie Sie)

- 20th ASEAN Working Group in Technical Cooperation in Pharmaceuticals (AWGTCP), 9 – 11 September 2003, Bali, Indonesia
  (Mrs Eishah Abdul Rahman, Dr. Sulaikah Moideen)

- WHO-ASEAN Harmonization of Regulatory Requirements Country Review Visit to Department of Drugs and Food, Ministry of Health, Kingdom of Cambodia, 2 - 8 November 2003
  (Mrs Noorizam Ibrahim).

- 6th International Training Course on the Use of Pharmacoeconomics in Drug Selection held on 13-23 September 2003 in Bangkok, Thailand
  (Mr Ramli Zainal)

- 26th Annual Meeting of Representatives of National Centres participating in the WHO Drug Monitoring Programme, New Delhi, India 8-10 December 2003
  (Mrs Abida Haq)

- The 5th International Conference on Traditional and Complementary Medicine (INTRACOM)

5.4 Training

5.4.1 Training for WHO Fellows

As a Collaborating Centre for WHO in Pharmaceutical Regulatory Control, the National Pharmaceutical Control Bureau (NPCB), Ministry of Health Malaysia continues to provide training services to fellows from other countries.

Malaysia received a total of 25 international visitors and WHO fellows from various countries namely Brunei Darussalam, Bangladesh, Bhutan, Islamic Republic of Iran, Papua New Guinea, Tongga, Uganda, United Arab Emirates, Vietnam and Sudan throughout the year 2003.

The courses provided under this programme are designed specifically to cater to the needs of the individual fellows. For personnel with laboratory background the courses include training in pharmaceutical analysis which includes dosage performance testing, chemical, microbiological, pharmacological and toxicological test methods, testing of traditional medicines as well as preparation and handling of reference standards. Other areas of training include aspects pertaining to GMP requirement and licensing system, drug registration, pharmacovigilance and post-marketing surveillance activities.

Details of the trainings provided by NPCB are as follows:

- Five WHO fellows from Vietnam i.e. Dr. Nguyen Tan Hai, Dr. Tran Thi Minh Huong, Dr. Luong Ngoe Khue, Miss Ha Manh Tuan, and Miss Le Thi Kim Thanh came for a study tour programme relating to management of rational drug use on the 28th of April 2003.

- Mr. Hamad Al Naemi, Director of the Department of Economy, United Arab Emirates (UAE) came for a study visit on the 15th of August 2003.

- Ms. Saffa Dawie from Sudan and Ms. Catherine Kafo from Tongga came for a study visit to the National Pharmaceutical Control Bureau on the 7th of April 2003 and 2nd of February 2003 respectively.

- Ms Noon Gar El Ghabar and Ms Iqbal Sid Ahmad Abdul El Rahim from Sudan was attached to the centre for a Study Tour Training Program on the Quality Assurance System in Malaysia from the 27th of January 2003 until the 26th of March 2003.

- Mr. Sherab Tenzin from Bhutan visited the centre for a Study Tour on Pharmacy at the National Pharmaceutical Control Bureau, 3 March 2003 - 23 May 2003.

- Ms. Balgess Abdul Bait from Sudan was attached to the centre for a Study Tour Training Program on the Quality Assurance System in Malaysia from 28 May 2003 – 28 July 2003.

- Mr. Chong Chee Kong and Dr. Dk Nurul Aina bte Pg Haji Md. Kilo from the Ministry of Health, Brunei Darussalam, did an attachment training on the Registration Process of Cosmetics by the National Pharmaceutical Control Bureau from the 3rd to the 15th of November 2003.

- Two WHO fellows i.e. Md. Mira Md. Aware and Md. Wahida Rahman from Bangladesh visited the centre for a Study Tour Program to study Good Manufacturing Practices

specifically for Training on Quality Control of Essential Drugs in Malaysia from the 21st of April 2003 until the 2nd of May 2003.

- Md. Nurul Islam Khan, a WHO fellow from Bangladesh did an attachment at the centre for a Study Tour Program on Good Manufacturing Practice (GMP) in Malaysia on the 2nd until the 26th of September 2003.

- The centre also received several official visits, including from:

  i) Mr. Said Heydary and Mr. Mahdian from the Islamic Republic of Iran on the 20th of October 2003.

  ii) Mr. Melchior Pep, Minister of Health of Papua New Guinea, accompanied by two of his officers on the 30th of October 2003.

  iii) Mr. Apollo and Ms. Florence from the Regulatory Agency of Uganda on the 29th of September 2003.

A summary of the visits received and trainings provided by NPCB are outlined in the table below:

TRAINING PROVIDED	NAME OF PARTICIPANTS	COUNTRY	DATE
Official visit to NPCB	1. Mr. Said Heydary 2. Mr. Mahdian	Islamic Republic of Iran.	20 October 2003
	1. Mr. Melchior Pep 2. PNG Ministry Officers 3. PNG Ministry Officers	Papua New Guinea (PNG)	30 October 2003
	1. Mr. Apollo 2. Ms. Florence	Uganda	29 September 2003
Study visit to NPCB	1. Dr Nguyen Tan Hai 2. Dr. Tran Thi Minh Huong 3. Dr Luong Ngoe Khue 4. Miss Ha Manh Tuan 5. Miss Le Thi Kim Thanh	Vietnam	28 April 2003
	Mr. Hamad Al Naemi	United Arab Emirates (UAE)	15 August 2003
	Ms. Saffa Dawie	Sudan	7 April 2003
	Ms. Catherine Kafo	Tongga	2 February 2003
Training program on Quality Assurance	1. Ms Noon Gar El Ghabar 2. Ms Iqbal Sid Ahmad Abd. El Rahim	Sudan	27 January – 26 March 2003
	Mr Sherab Tenzin	Bhutan	3 March - 23 May 2003
	Ms Balgess Abdel Basit	Sudan	28 May – 28 July 2003
	1. Mr. Chong Chee Kiong 2. Dr. Dk Nurol Aini bte Pg Haji Md. Kifli	Brunei	3 – 15 November 2003
Good Manufacturing Practice	1. Md. Mirza Md. Anwarul 2. Md. Md Wahidur Rahman	Bangladesh	21 April 2003 – 2 May 2003
	Md. Nazrul Islam Khan	Bangladesh	2 - 26 September 2003

5.4.2 Centre's Staff Development

In 2003, officers from the centre also underwent various training courses to upgrade and improve their knowledge and skills both within the country and internationally.

Post-Graduate Studies

The following staffs are pursuing further studies in 2002-2004

- Hasenah bt Ali (Ph. D candidate, King's College, University of London UK)
- Kamaruzaman b Saleh (Ph. D candidate, Universiti Sains Malaysia)
- Ainul Salhani bt Abdul Rahman (M. Sc. Candidate, University Putra Malaysia)

The following staffs are pursuing further studies in 2003-2006

- Ramli Zainal (Ph. D candidate, Universiti Sains Malaysia)
- Noorul Akmar bt. Mohd. Nur (Ph. D candidate, Universiti Sains Malaysia)
- Roshayati Mohd. Sani (Ph. D candidate, Universiti Sains Malaysia)

Short Courses/Training at International Level

- Mrs Abida Haq underwent attachment training pertaining at the Therapeutic Goods Administration, Australia 28 April – 9 May 2003 to get hands-on experience in matters pertaining to surveillance of drugs and medical devices, drug recall procedures as well as to get an in-depth knowledge on the Australian Adverse Drug Reactions Monitoring System
- Mrs Rohani Ismail was attached to the Australian Pesticides & Veterinary Medicines Authority, Australia 28 April – 9 May 2003 to get training pertaining to the Australian registration system of veterinary medicinal products as Malaysia will also be embarking on the registration of veterinary products in 2004
- Mrs Arpah Abbas attended the WHO Global Training Network Course on Vaccine Regulation for National Control Authorities conducted at the Therapeutic Goods Administration, Canberra, Australia to gain knowledge on the evaluation of vaccines

Local Short Courses/Training

Many of the Centre's staff had the opportunity to attend various courses and training programs which were held within the country pertaining to drug evaluation, analysis and regulation.

- International Course on Regulatory Drug Evaluation
- Evaluation of Analytical Method Validation Data
- Good Clinical Practice (GCP) Audits
- Formulation of Strategies to Promote and Strengthen the Implementation of Bioequivalence Studies in Malaysia
- Herbal and Phytochemical Processing
- LAL Seminar
- National Conference on Biotechnology & Life Sciences
- Regulation & Control Of Blood Products
- Compliant Filtration for Biopharmaceutical Industry
- Global GMP & Regulatory Update
- The 2nd Asian Regional Health Technology Assessment Conference

5.5 Participation in Activities Coordinated By Other Countries/Organisations –

Production and Utilization of ASEAN Reference Standards

The development of reference substances was also given due consideration. NPCB had obtained special funding and was allocated RM 0.5 million for the purchase of new analytical

equipment and RM 1 million for the purchase of primary reference standards in an effort to further strengthen the activities of the Reference Standard Unit.

The NPCB which represents Malaysia as a member in this collaborative project has sent to Singapore (Health Sciences Authority) and the Philippines (Bureau of Food and Drugs) in mid 2002, portions of the 3 proposed ASEAN Reference Substances (ARS) bulk material namely, Riboflavin, Methylparaben, Propylparaben and their respective primary standards and protocols of analysis required for the studies. The completed analytical reports from these 2 laboratories along with the one from us as the coordinating country, were then compiled and collated for the purpose of submission to the adoption meeting, held in Thailand in February 2003.

The 12th Meeting on the Production and Utilization of ASEAN Reference Substances was held on the 11-13th February 2003 at the Department of Medical Sciences, Ministry of Public Health, Thailand. Malaysia was represented by Mr. Muhammad Nasir Hashim of the NPCB. At the meeting, Methylparaben and Riboflavin were adopted as ASEAN Reference Substances, while Propylparaben was put on hold pending further test results from the Philippines, which at the time of this report writing, has been made available. Eleven (11) substances with a mixture of new and 2nd/3rd batches were suggested by Malaysia at the meeting for the next coming production and collaborative studies and they are as follows:

1. Betamethasone Dipropionate
2. Prednisolone
3. Norfloxacine
4. Guaifenesin
5. Prednisone
6. Cephalexin
7. Cyanocobalamine
8. Erythromycin
9. Nystatin
10. Lignocaine
11. Diphenhydramine Hydrochloride

By early June 2003, Malaysia completed the collaborative analysis on the Proposed ASEAN Reference Substance (PARS), ibuprofen, which was handed by the coordinating country Philippines during the 12th Meeting, held in February 2003 in Bangkok.

In July 2003, 5 vials each of Hyoscine Butylbromide and Hyoscine Hydrobromide ARS were delivered to Thailand. The Japan Pharmaceutical Manufacturers Association (JPMA), through the Society of Japanese Pharmacopoeia (SJP) had sent Prednisolone (200g) and Nystatin (300g) raw materials to Malaysia for the next coming PARS collaborative studies.

6. Updates on Regulatory Control

Up to December 2003, a cumulative total of 79,295 product applications for registration have been received, of which 35,628 have been approved.

The following are the breakdown for the type of applications received in the year 2003 -

- Scheduled poisons - 175
- Non-scheduled poisons - 266
- Cosmetics - 26,177
- Traditional medicines - 1,491

A total of 2,410 Certificates of Pharmaceutical Product (CPP) and 1,309 Certificates of Free Sale (CFS) were issued for the year 2003.

From a of total 217 licensed Manufacturers, 176 manufacturing facilities premises were inspected by the centre's GMP auditors to ensure compliance to GMP standards.

A total of 2037 products were sampled up under the post-market surveillance program to establish compliance to regulatory requirements.

The drug analysis division tested a total of 4180 samples ,of which 2420 were registration samples,1337 were surveillance samples and 413 were queried/ Enforcement samples. A total of 51251 tests were conducted.

A total of 233 vials of ASEAN and NPCB reference standards were supplied to government departments (Chemistry Department, Government Medical Store Sarawak and State Enforcement Units) and a total of 425 vials were sold to the private sector.

Under the Adverse Drug Reactions Monitoring Program, a total of 1067 reports were received during 2003 of which 901 reports which were evaluated and sent to the Uppsala Monitoring Centre for inclusion into the WHO database.

The centre also responded to 1336 queries for product information from both the public and private sectors.

7. Future Directions

- **Expansion of Product Registration** : to implement registration of veterinary medicines and active pharmaceutical ingredients, to continue participation in global harmonization for pharmaceuticals, cosmetics, to improve the current work-processes

- **GMP Benchmarking**: to strengthen efforts to upgrade the level of GMP compliance of local pharmaceutical and traditional medicines industries, to gain mutual recognition of GMP with PIC/S, FDA, TGA and ASEAN, to develop pool of local experts in GMP, to export technical and professional services in GMP and licensing

- **Post-market surveillance**: to combat problems associated with adulteration, counterfeit and authentication of registered products, promote public health protection via education and awareness

- **Detection method for adulterants in traditional medicine:** to offer training on the analytical system for the detection of adulterants in traditional preparations.

- **Information and Communication Technology (ICT)**: to implement on-line registration of traditional medicines and New Chemical Entities, electronic ADR monitoring, on-line drug information services, establish information kiosks/on-line product registry , networking with enforcement units via electronic palm-devices

- **New ISO 9000 Certification**: to achieve the ISO 17025 for the laboratory services