1.0 INTRODUCTION

A company applying to the National Pharmaceutical Control Bureau (NPCB) for the registration of a medicinal product in Malaysia must provide acceptable evidence to show that the manufacturer of the product follows an internationally accepted standard of Good Manufacturing Practice (GMP) and recognized by the authority in Malaysia.

The Control of Drugs and Cosmetics Regulations 1984 (CDCR) requires that the standard of manufacture and quality control of medicinal products manufactured outside Malaysia be taken into consideration before the products are registered with the authority namely Drug Control Authority (DCA). NPCB as the secretariat to the DCA is responsible to ensure all manufacturers of registered products in Malaysia are able to provide acceptable evidence that the manufacturing premises conform to current GMP requirements. Hence, foreign manufacturers are also subjected to GMP conformity assessments through acceptable GMP evidence or GMP inspection.

Malaysia became the 26th member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) since 1st January 2002. Hence, the current PIC/S Guide to GMP for Medicinal Products and its Annexes have been adopted as the standard used by NPCB to assess the GMP conformity of manufacturers.

2.0 DEFINITIONS/ABBREVIATIONS

GMP	:	Good Manufacturing Practice
NPCB	:	National Pharmaceutical Control Bureau
CDCR	:	Control of Drugs and Cosmetics Regulations 1984
DCA	:	Drug Control Authority
PIC/S	:	Pharmaceutical Inspection Co-operation Scheme (Information on PIC/S Participating Authority can be accessed on the PIC/S website – www.picscheme.org)
ICH	:	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (Information on ICH can be accessed on the ICH website – www.ich.org)

ICH member country	:	Japan, Member of the European Union (EU) and United States of America (USA)
SMF	:	Site Master File
VMP	:	Validation Master Plan
LOC	:	Letter of Confirmation
CAPA	:	Corrective Action and Preventative Action
MOH	:	Ministry of Health Malaysia

3.0 PURPOSE

3.1 The objective of the foreign GMP inspection is to ensure the conformance of foreign manufacturers to GMP requirements and standards for products that are registered or that are undergoing the registration/re-registration/change of manufacturing site process with the DCA of Malaysia and those products manufactured for clinical trial purposes (investigational medicinal products) with a view to strengthen the supervision and administration over the imported products as well as regulating the manufacture and ensuring the quality and safety of the imported products.

3.2 The purpose of this guidance is:-

3.2.1 to provide information on the types of GMP evidence acceptable to the DCA of Malaysia.

3.2.2 to provide the requirements for an on-site inspection of the manufacturing facilities outside Malaysia where the GMP evidence of the premise is not available or acceptable to the DCA of Malaysia.

3.2.3 to provide guidance on how to apply for an on-site foreign GMP inspection.

4.0 SCOPE

4.1 This guidance applies to all manufacturers of medicinal products located outside Malaysia.

5.0 ACCEPTABLE GMP EVIDENCE

5.1 One of the requirements to register an imported medicinal product in Malaysia is the submission of acceptable documentary evidence on the GMP compliance of the manufacturer.

5.2 NPCB will accept documentary evidence of GMP conformance of a manufacturer located outside Malaysia on the following condition:

5.2.1 The GMP evidence is issued by a PIC/S Participating Authority or an ICH member country Competent Authority following an on-site inspection conducted by the authority; OR

5.2.2 The GMP evidence is issued by a Listed Inspection Service under the ASEAN Sectoral Mutual Recognition Arrangement for Good Manufacturing Practice (GMP) Inspection of Manufacturers of Medicinal Products.

5.3 The acceptable GMP evidence issued by the authority as mentioned in para 5.2 shall be in the format of:

5.3.1 GMP certificate
5.3.2 GMP inspection report

5.4 Where acceptable GMP evidence of the foreign manufacturer is not available, or where the documentary evidence submitted is insufficient to demonstrate acceptable GMP standard, **a GMP inspection has to be conducted on the manufacturer by NPCB**.

5.5 The availability of acceptable GMP evidence does not preclude NPCB from carrying out the GMP inspection on the manufacturer.

6.0 GENERAL REQUIREMENTS AND PROCEDURES FOR THE APPLICATION OF A FOREIGN GMP INSPECTION

*Please refer to Annex I for an overall process flow for the application of a foreign GMP inspection

Application of foreign GMP inspection

6.1 The application for a foreign GMP inspection should be made by a Malaysian registered company acting on behalf of the foreign manufacturer.

6.2 The Malaysian registered company (Product Registration Holder) shall authorize a responsible person (e.g. Chief Executive Officer, Managing Director or Regulatory Manager) to act as the liaison officer with NPCB for all arrangements pertaining to the proposed inspection.

6.3 The appointed liaison officer responsible for the application is required to submit the completed application form (BPFK 501) with the necessary supporting documents such as the current version of Site Master File (SMF) and Validation Master Plan (VMP).

6.4 No payment is required at this stage of application.

6.5 If the application is successful, NCPB will write to the applicant and announce the proposed date and duration of inspection. Following this process, the applicant shall then submit a completed Pre-Inspection Form (BPFK 502) together with required information on travel and accommodation.

6.6 Using the information obtained from the applicant, NPCB will calculate the total inspection cost and inform the applicant accordingly.

6.7 Prior to conducting the inspection, a meeting will be organized between the appointed GMP inspectors and the applicant for preparation of the inspection. Subsequent meetings shall be organized by the lead inspector if necessary.

Transportation and accommodation

6.8 Travelling arrangement includes both ground travel and air travel. The applicant is expected to propose a suitable flight itinerary to NPCB based on the following criteria:

6.8.1 Flight is of the shortest distance from Kuala Lumpur to the point of destination and without transit. If transit is required due to unavailability of routes, the details of the transit destination and duration should be included.

6.8.2 Flight class is economy class, with fare structure allowing for change of flight date and time without any fee.

6.8.3 Preferred airline operator is Malaysian Airline System Berhad ("Malaysia Airlines").

6.9 The information on accommodation will be required in the form of an official quotation or similar and satisfy the following criteria:

6.9.1 Hotel room category is Standard Room.

6.9.2 Reasonable distance between hotel and the manufacturing facility (Please state the estimated duration to reach the manufacturing facility from the hotel).

Inspection Fee and Inspection Expenses

6.10 The payment structure for the foreign GMP inspection consist of two parts, in which both shall be borne by the applicant as follows:

6.10.1 Inspection Fee

a) The inspection fee for a foreign manufacturing facility is EURO 5,000.

b) NPCB will issue an invoice to the company **one month before** the foreign inspection is conducted.

c) The payment for the inspection fee must be made at least **one week before** the foreign inspection is conducted.

d) The payment shall be made using a banker's cheque payable to:

Name	:	**BIRO PENGAWALAN FARMASEUTIKAL KEBANGSAAN, KEMENTERIAN KESIHATAN MALAYSIA**

e) The payment for the inspection fee is non-refundable in any circumstances.

6.10.2 Inspection Expenses

a) The inspection expenses will cover all the expenses incurred to conduct the inspection which include flight ticket, accommodation, and other associated expenses (such as allowances, insurance, etc.)

b) The costing will be prepared by NPCB, based on the eligibility of the inspectors as outlined in the Treasury Circular 3/2003 issued by the Malaysian Ministry of Finance.

c) Payment for the inspection cost shall be in the form of contribution into a trust fund established under the Malaysian Ministry of Health (MOH) namely *Akaun Amanah Penilaian, Pengiktirafan Akreditasi dan Pemeriksaan APB* (Main Code: 886341, Sub Code: 4001) through a **banker's cheque** made payable to:

Name	:	**KETUA SETIAUSAHA KEMENTERIAN KESIHATAN MALAYSIA**
Account No	:	**21401360003459**

d) The expenses for the inspection will be covered using the contribution from the trust fund as mentioned in 6.10.2(c). NPCB will table the inspection expenses to MOH Trust Fund Committee for approval before the fund can be used.

e) The remainder of the contribution will be retained in the trust fund for future purposes as outlined in the *Arahan Amanah Penilaian, Pengiktirafan Akreditasi dan Pemeriksaan APB.*

f) However, in the event where the foreign GMP inspection cannot be conducted, the contribution will be refunded.

Outcome of Inspection

6.11 The outcome of the GMP inspection will be tabled to the Committee of Evaluation of Inspection on Premises.

6.12 The GMP inspection report will be issued to the manufacturer through the applicant **within 20 working days** after the acknowledgement of the GMP inspection outcome of the manufacturer by the Committee of Evaluation of Inspection on Premises.

6.13 The manufacturer is required to submit a Corrective Action and Preventative Action (CAPA) report to NPCB for the findings reported during the inspection within 30 days of receiving the GMP inspection report. The CAPA proposal will be presented to the Committee of Evaluation of Inspection on Premises for further consideration.

6.14 The GMP compliance will only be concluded once all CAPA have been closed out. All CAPA needs to be closed out within 6 months from the date the inspection report is issued, otherwise the GMP compliance is deemed to be unacceptable.

6.15 If the GMP compliance is concluded as acceptable, NPCB will issue a GMP certificate to the manufacturer through the applicant. The GMP certificate shall be used administratively for the purpose of product registration/re-registration/change of manufacturing site with NPCB.

6.16 If the GMP compliance is concluded as unacceptable, there will be no further consideration or appeal for the GMP compliance of the manufacturer. The applicant has to submit a new application in order for NPCB to conduct another inspection on the manufacturer.

Additional Information

6.17 The date of the inspection will be assigned according to first-come-first-serve basis upon receipt of a completed application form (BPFK 501).

6.18 The applicant shall submit a written application, explaining the reason, to NPCB if there is a reason for postponing the inspection. However, the inspection will be cancelled if the postponement is made after Form BPFK 502 has been submitted.

6.19 The GMP inspection is still subject to final approval by the Ministry of Health Malaysia and Ministry of Finance Malaysia.

6.20 The applicant is required to arrange for a translator to be made available during the on-site inspection, at the company's cost, if English or Bahasa Malaysia is not the language used in communication and documentation by the foreign manufacturer.

6.21 The applicant is also required to assign an individual from the Product Registration Holder company to accompany the GMP inspectors during the whole duration of the inspection.

6.22 The manufacturer must ensure that any translated version of documentation that are provided to the GMP Inspector during the inspection is clear, legible, accurate and in official manner, in line with the manufacturers documentation system.

6.23 The manufacturer shall operate and run production activities as usual during the inspection.

6.24 The number of inspectors appointed and duration of inspection will be decided upon by the NPCB depending on the nature of the products, size of the premises to be inspected and scope of the inspection. In normal circumstances, the minimum number of inspector is 3 inspectors for a minimum duration of 3 days.

6.25 Inspections are limited to one inspection site, and either sterile or non-sterile facility, per inspection only. Inspections to multiple sites or to both sterile and non-sterile facilities will require separate applications.

6.26 NPCB adopts the PIC/S Guide to GMP for Medicinal Products and its annexes for the GMP inspection.

6.27 NPCB reserve the right to invalidate the GMP certificate issued to the manufacturer when evidence exists (such as product complaints, serious adverse events, etc.) or NPCB have reason to believe that the manufacturer is not complying with the GMP guidelines/requirements.

6.28 The same GMP certificate may be used by the same applicant for other product registration applications if the scope of manufacture is the same, provided the validity date of the GMP certificate is still current.

6.29 An acceptable GMP compliance of a manufacturer does not guarantee the manufactured product will be approved for registration in Malaysia.

6.30 Enquiries relating to foreign GMP inspection may be directed to the following contact:

Centre for Compliance and Licensing
National Pharmaceutical Control Bureau
Ministry of Health Malaysia
Lot 36, Jalan Universiti,
46200 Petaling Jaya, Selangor.

Tel : (60)-378835565
Fax : (60)-379571200

7.0 ANNEXES

Annex I - Process Flow: Foreign GMP Inspection

8.0 FORMS

BPFK 501 - Foreign GMP Inspection Application Form

BPFK 502 - Foreign GMP Inspection Pre-Inspection Form

9.0 REFERENCES

9.1 *Direktif Mengenai Syarat Pendaftaran Produk Farmaseutikal Dari Luar Negara Berkaitan Keperluan Amalan Perkilangan Baik (APB), Bilangan 1 Tahun 2012*

9.2 *Pekeliling Perbendaharaan Bilangan 3 Tahun 2003*

10.0 END OF DOCUMENT

This guidance document replaces the previous version of similar guide titled 'Guidance Document on GMP Audit of a Foreign Manufacturer'.

Process Flow: Foreign GMP Inspection