GMP for Imported Products - Foreign GMP Regulatory Inspection

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NPRA MALAYSIA NATIONAL PHARMACEUTICAL REGULATORY AGENCY

MINISTRY OF HEALTH MALAYSIA

WHO Collaborating Centre for Regulatory Control of Pharmaceuticals

Member of Pharmaceutical Inspection Co-operation Scheme

Certified to ISO 9001:2008 Cert. No.: AR 2293

NO: SAMM 450

Member of OECD

PRESENTATION OUTLINE

- Introduction
- GMP Evidence
- Directives On Acceptable GMP Evidence
- Foreign GMP Inspection
- Guideline
- Statistic of Foreign Inspections

INTRODUCTION

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 Drug Control Authority (DCA).

INTRODUCTION

NPRA as the secretariat to the DCA is responsible for ensuring;

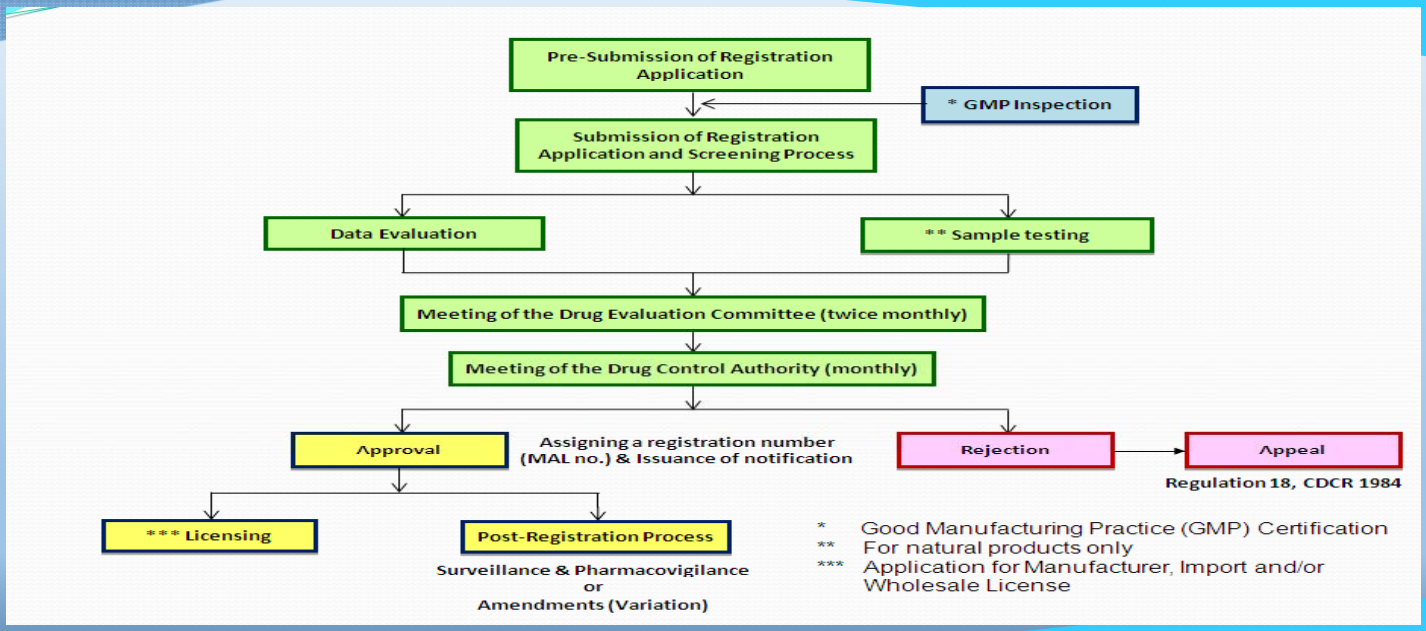
- All manufacturers of registered products in Malaysia are able to provide acceptable evidence that the manufacturing premises conform to current GMP requirements. \
- Hence, foreign manufacturers are also subjected to GMP conformity assessments through **acceptable GMP evidence or GMP inspection by NPRA**.

INTRODUCTION

Malaysia (NPRA) became the **26th member of the PIC/S** since 1st January 2002.

Therefore, **the current PIC/S Guide to GMP for Medicinal Products and its Annexes** have been adopted as the standard used by NPRA to assess the GMP conformity of medicinal product manufacturers.

Product Registration Process



PHARMACEUTICAL PRODUCTS

Pharma product registered in Malaysia; (march 2016)

Total Products Registered	: 24,700
Local Manufactured	: 40 %
Imported	: 60 %

*Source: NPRA

GMP EVIDENCE

1. One of the requirements to register/renew the registration of an imported medicinal product in Malaysia is submission of acceptable evidence of the GMP Compliance of the manufacturer.

2. This GMP evidence is also required as supporting documents for application of change of site (COS) for the purpose of verifying the GMP status of the foreign manufacturer.

ACCEPTABLE GMP EVIDENCE

For pharmaceutical manufacturer **located out site Malaysia**, GMP complians status is verified through.

- **GMP Certificate**
- **GMP Inspection Report**

GMP CERTIFICATES

A GMP certificate is granted when the manufacturing facility has been audited and found to demonstrate satisfactory compliance with the required GMP standard.

A GMP certificate would normally be valid for 3 years from the date of inspection/assessment

Example:
Date of inspection: 01/01/2013
Date of GMP certificate evaluation: 02/01/2016
** GMP certificate will consider not acceptable.

GMP INSPECTION REPORT

- Brief summary of the manufacturing activities.
- Brief description of the quality management system of the firm
- Brief summary of the findings, and recommendations (where applicable).
- Conclusion regarding the GMP status.

GMP report serves as supporting document for the regulator to clarify information which is not mentioned in GMP certificates.

GMP EVIDENCE

What NPRA will look into when evaluating GMP certificate/reports

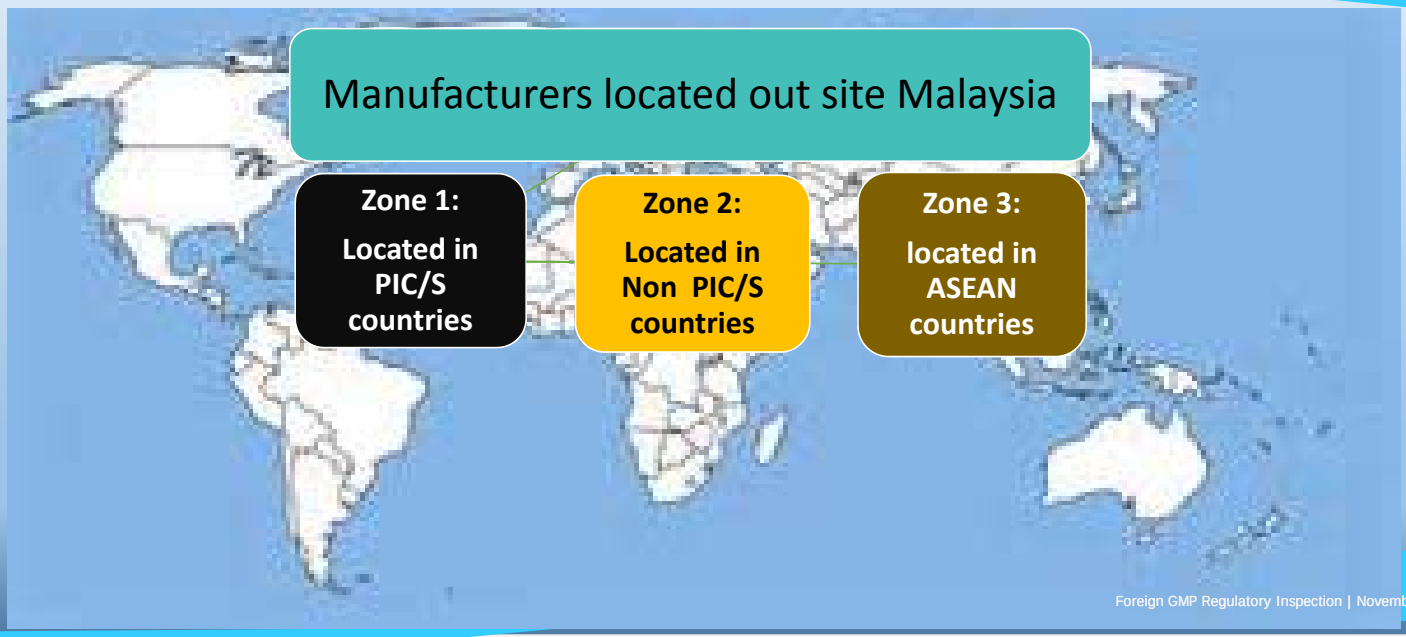
- Issuing authority
- Name and address of the manufacturing site
- Date of inspection
- Types of dosage forms/range of products being manufactured
- GMP standard used for the inspection
- Clarifying remark/restriction: Penicillin & Non penicillin block, steroids & non-steroids block

ACCEPTABLE GMP EVIDENCE

Acceptance of GMP evidence.

- Issued by the NDRA that regulates the products
- Based on their latest GMP routine inspection (< 3yrs)
- **GMP Inspection conducted against the PIC/S GMP Guides**

FOREIGN MANUFACTURERS



DIRECTIVES ON FOREIGN GMP INSPECTIONS

Directive: No. 1 /2012

- Directive: Requirement of GMP for Registration of Imported Pharmaceutical Products.

Directive: No. 1/2016

- Directive: Requirement for Foreign GMP Inspection for the New /Renew Registration of Pharmaceutical Products.

Directive: No. 11 /2016

- Directive: Acceptance of GMP Complians for the Renewal Registration of Pharmaceutical Products.

DIRECTIVES ON FOREIGN GMP INSPECTIONS

Directive:
No. 1 /2012

Directive: Requirement of GMP for Registration of Imported Pharmaceutical Products.

- For New Registration & Renewal Registration:
- For facilities located in PIC/S or ICH countries:
  - GMP Certificate/Inspection report
- For facilities located in Non PIC/S or Non ICH countries but have been inspected by NDRA of PIC/S or ICH:
  - GMP Certificate/Inspection report
- No GMP Inspection by NPRA

DIRECTIVES ON FOREIGN GMP INSPECTIONS

Directive:
No. 1 /2016

Directive: Requirement for Foreign GMP for the New/Renew Registration of Imported Pharmaceutical Products.

- For facilities located in Non PIC/S or Non ICH countries:
  - For new registration:
    - Inspection by NPRA is REQUIRED effective: July 2016
  - For renewal registration:
    - Inspection by NPRA is REQUIRED effective: January 2017.

DIRECTIVES ON FOREIGN GMP INSPECTIONS

Directive:
No. 11 /2016

Directive: Acceptance of GMP Complians for the Renewal Registration of Pharmaceutical Products

- For renewal registration:
- For facilities located in non PI/CS or Non ICH countries but have been inspected by NDRA of Reference Countries* :

- Inspection by NPRA is NOT REQUIRED effective: January 2017.

FOREIGN GMP INSPECTION

For the registration of pharmaceutical products from the manufacturers **located out site Malaysia**, GMP inspection by the NPRA is **NOT REQUIRED** for:

Manufacturers located in PIC/S countries

Manufacturers located in Non PIC/S countries but certified by NDRA from Reference Countries*

(for renewal only)

Manufacturers located in ASEAN countries and certified by NDRA Listed Inspection Service under the ASEAN Sectoral MRA on GMP

FOREIGN GMP INSPECTION -OBJECTIVE

1. Assess the **conformance of foreign manufacturers to GMP requirements.**

2. Ensure **quality and safety of products** that are registered or in the process of registration/re-registration/change of manufacturing site with DCA of Malaysia and products manufactured for clinical trial purposes (investigational medicinal products).

3. This activity is to strengthen the **supervision and administration** over imported products and foreign manufacturers.

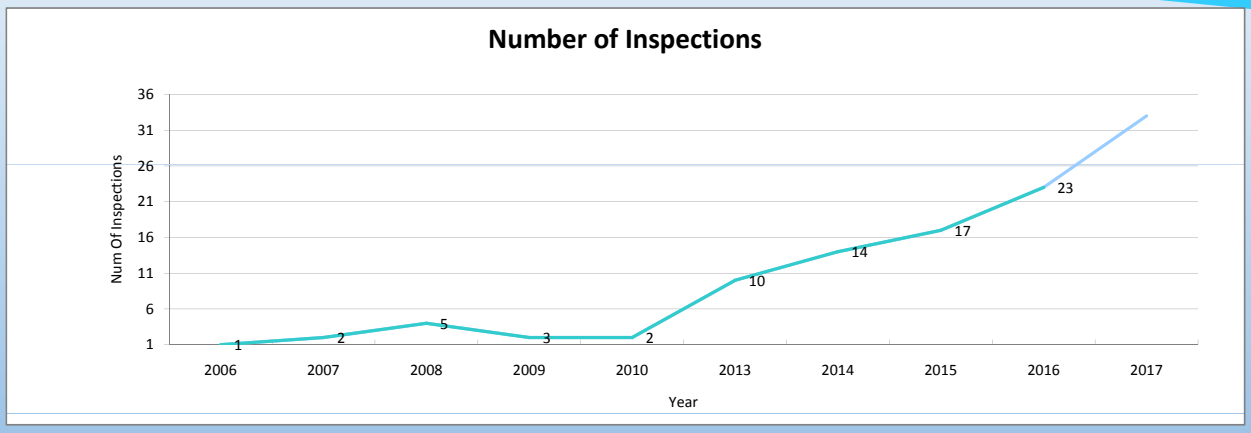
GUIDELINE

GUIDANCE DOCUMENT FOREIGN GMP INSPECTION

2nd Edition

July 2016

STATISTIC OF INSPECTIONS



70 inspections have been conducted by NPRA until the date of 25/10/16 while 7 inspections are scheduled to be conducted before 31/12/16.

*Source: NPRA

STATISTIC OF INSPECTIONS

FOREIGN GMP INSPECTION

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	TOTAL
Pharma	0	1	1	2	2	0	0	6	13	15	17	**67**
Biological	0	0	0	1	0	0	0	4	0	2	5	**12**
Traditional / Health Supp.	1	1	4	0	0	0	0	0	1	0	1	**8**
TOTAL	**1**	**2**	**5**	**3**	**2**	**0**	**0**	**10**	**14**	**17**	**23**	**77**

*Source: NPRA

STATISTIC OF INSPECTIONS

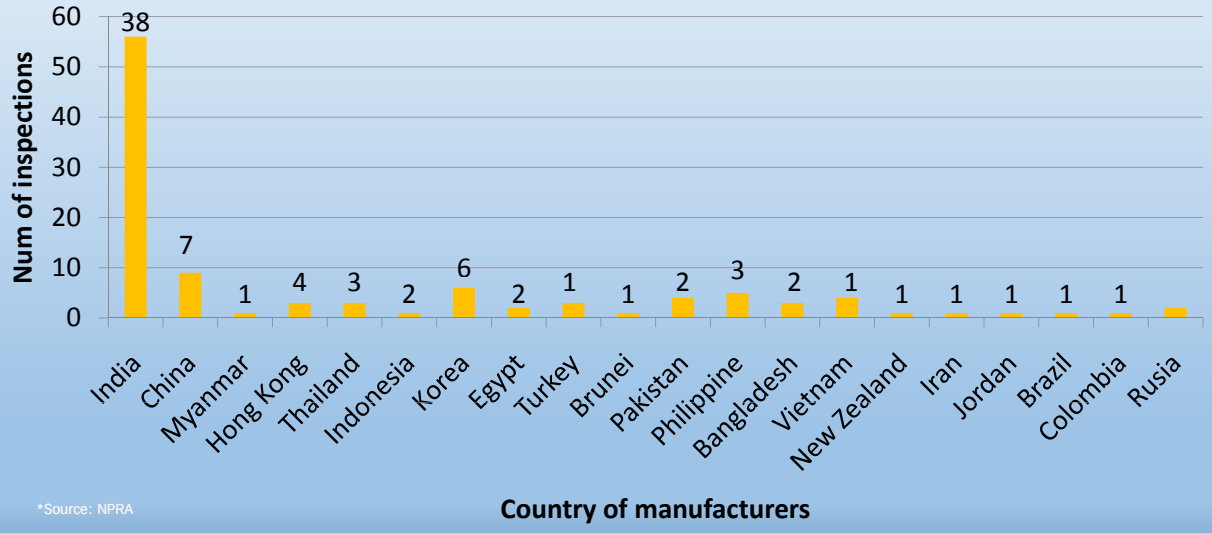
FOREIGN GMP INSPECTION

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	TOTAL
Sterile	0	1	1	3	2	0	0	10	4	7	11	**39**
Non Sterile	1	1	4	0	0	0	0	0	10	10	12	**38**
TOTAL	**1**	**2**	**5**	**3**	**2**	**0**	**0**	**10**	**14**	**17**	**23**	**77**

*Source: NPRA

STATISTIC OF INSPECTIONS

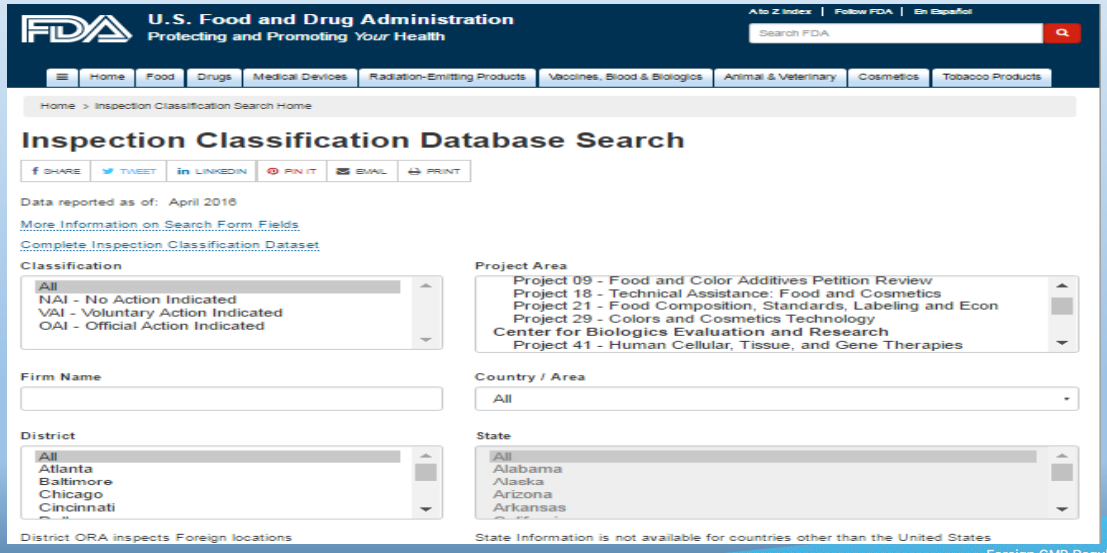
Location of Manufacturers



*Source: NPRA

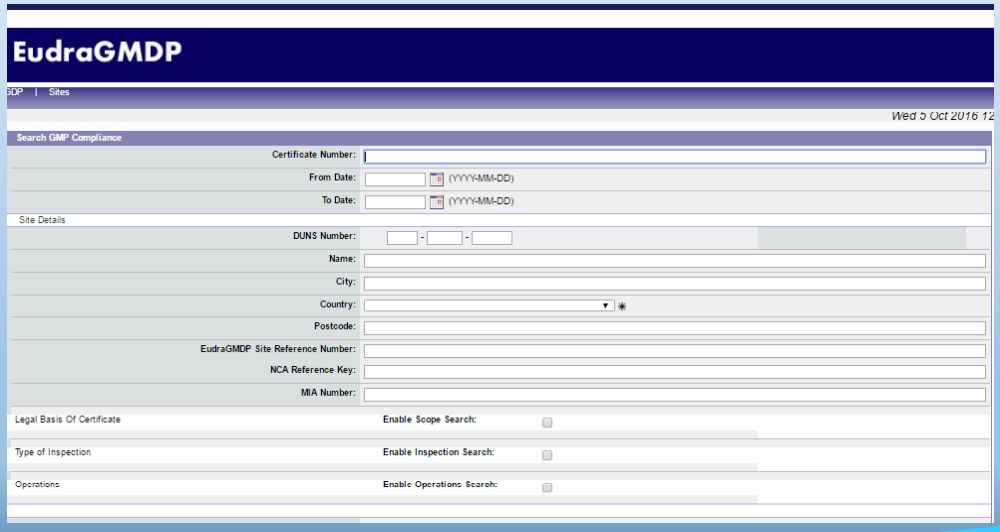
Some useful link to check on GMP validity

US FDA - http://www.accessdata.fda.gov/scripts/inspsearch/



Some useful link to check on GMP validity

http://eudragmdp.ema.europa.eu/inspections/gmpc/searchGMPCompliance.do



More info….

http://npra.moh.gov.my