APAC
Asia Partnership Conference of Pharmaceutical Associations

6th APAC meeting at ATIM session

Assessment Process of GMP Compliance in Taiwan

Current status & Future possibility

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FDA Food and Drug Administration

http://www.fda.gov.tw/

Outline

GMP Compliance of Medicinal Products in Taiwan

- Regulatory System
- Assessment of GMP Compliance
- Process for Foreign Manufacturers
- Moving Forward

Outline

GMP Compliance of Medicinal Products in Taiwan

Regulatory System

- **Legislative Framework**
- **Competent Authority**
- **Adopt & Adapt the PIC/S GMP**

Legislation Framework

Pharmaceutical Affair Act (PAA)

§57 **Guide to GMP for MPs & MDs**

The manufacturing of modern MPs shall comply with the **PIC/S GMP Guide**

§57 **Regulations for Issuance of Manufacturing Licenses**

§71 **Regulations for Inspection**

New GMP assessment,
Routine inspection (2 to 4-year cycle)
For-cause inspection

Article 57 of PAA

- The manufacturing of medicinal products (MPs) & medical devices(MDs) shall comply with the Good Manufacturing Practice requirements (including export only)
- The Manufacture of MPs & MDs must be authorized based on GMP inspections by Central Health Authority.
- these requirements apply to the foreign manufacturer of imported products.

Article 92 of PAA

- Health Authority has legal power to suspend, revoke or amend a manufacturing license.

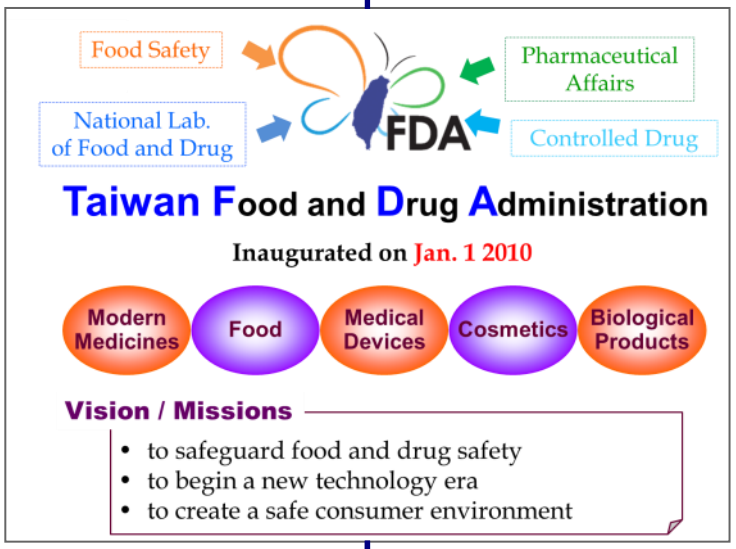
Article 71 of PAA

- give Health Authority the legal power to inspect the sites….

Competent Authority – Taiwan FDA

A member of PIC/S starting on Jan. 1, 2013

Ministry of Health and Welfare



Div. of Drugs

Product License

Div. of Risk Management

Manufacturing License

GXP Inspectorate (GMP/GTP/GDP/GLP)

- **Pharmaceutical GMP Inspection and Licensing System** has been established based on:
  - PIC/S Recommendations (PI 002-3)
  - ICH Q10, ICH Q9
  - ISO 9001:2008, ISO 19011:2002, ISO17020:1998
- **Competent inspectors**

  Qualification & training
- Quality manual, SOPs, work instructions

Adopt the PIC/S GMP

Publish **bilingual version** of PIC/S GMP Guide

西藥藥品優良製造規範

（第一部、附則）

PIC/S：Guide to Good Manufacturing Practice for Medicinal Products

（Part I、Annexes）

PE009-12 (1 October 2015)

© PIC/S October 2015

第一章　品質管理（QUALITY MANAGEMENT）

原則（PRINCIPLE）	
製造許可的持有者製造藥品時，應確保該藥品適合其預定用途，符合上市許可的要求，且不會由於安全性、品質或有效性的不足而使病人陷於危險。該品質目標之達成是高層管理者的責任，且需要公司內各部門及所有階層之人員，以及公司之供應商與經銷商的參與和許諾。	The holder of a manufacturing authorisation must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorisation and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment by staff in many different departments and at all levels within the company, by the company's suppliers and by the distributors.
為可靠達成該品質目標，應有全面設計並正確實施的品質保證系統，該系統並應完整實施良製造規	To achieve the quality objective reliably there must be a comprehensively designed and

- Current version : PE009-12, 1st October 2015.
- The translation of newest version of PIC/S GMP Guide (PE009-13, 1st Jan. 2017) is in progress

GMP
1982~

cGMP
(validation)
1995~

PIC/S GMP
2007.12~

衛生福利部 食品藥物管理署 FDA Food and Drug Administration

Adapt the PIC/S GMP

Dec. 2007

Announced the timeframe to implementing the PIC/S GMP

- **new** facilities, expansion, new production line have to comply with PIC/S GMP

2015.1.1

All manufacturers of modern medicinal products shall fully comply with PIC/S GMP

- For those facilities which are unable to comply with PIC/S GMPs, its manufacturing license had been revoked & importation of MPs was prohibited.

2010.1.1

PIC/S GMPs has been used for all of the inspections

Training for Industry (free)

2016.1.1

All manufacturers of APIs shall fully comply with the PIC/S GMP

Outline

GMP Compliance of Medicinal Products in Taiwan

Assessment of GMP Compliance

- **Domestic manufacturers**
- **Foreign manufacturers**

Assessment of GMP Compliance

- Domestic Manufacturers -

Linked to issuance & renewals of Manufacturing License(has expiry date)

Inspected On-Site

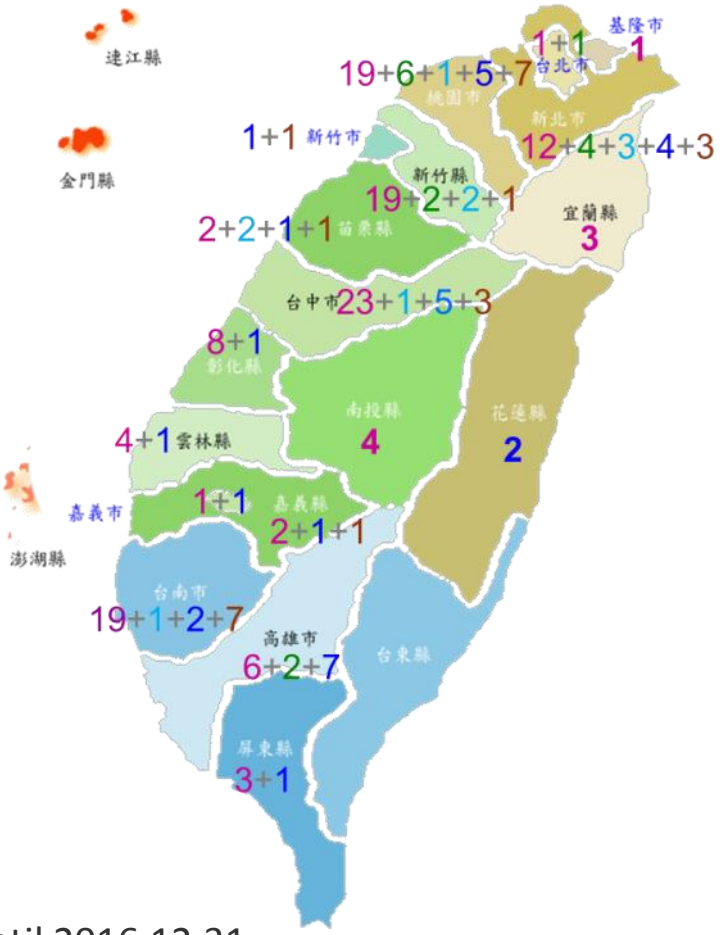
- Manufacturers of MPs
- Logistics company/ Wholesaler which involved packaging & labeling of MPs
- APIs manufacturers
- Medical gases manufacturers
- Contract laboratories

Types of Inspection

- **GMP assessment** of New facilities, relocation and expansion of existing facilities, resumption of operations, Addition of new dosage forms
- **Routine inspection** 2-4 years, adjusted based on risk
- **For-cause inspection** without notification

Authorized Pharmaceutical Manufacturers in Taiwan

- **208** sites in total
  - **127** manufacturers of MPs
  - **15** logistics companies involve in packaging & labeling of MPs
  - **10** pilot plants for IMPs
  - **32** Medicinal Gas manufacturers
  - **24** APIs manufacturers



data collection until 2016.12.31

Assessment of GMP Compliance

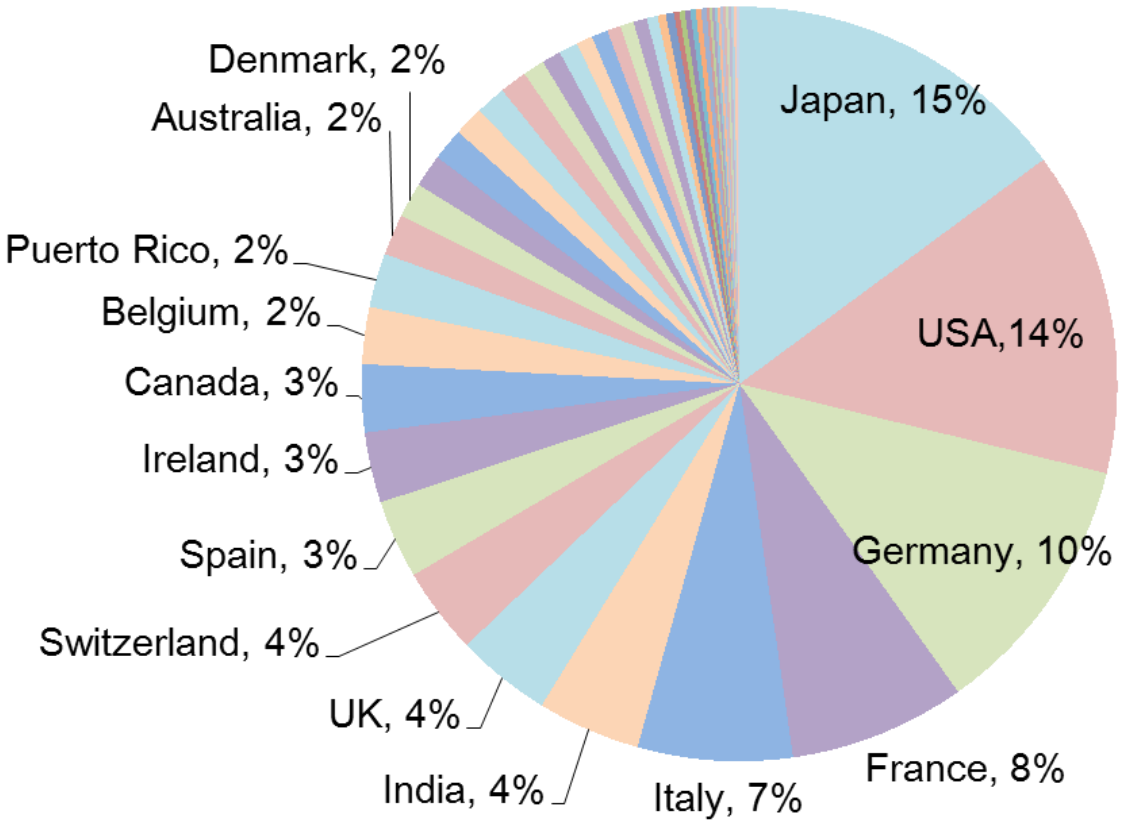
- Foreign Manufacturers -

- An **Official Letter of GMP compliance** (has expiry date) issued by the Taiwan FDA /MoHW is requested for product registration.
- The application could only be submitted via the **Taiwan sponsor**, who must get a Drug Dealer License issued by Taiwan health authority.
- Evidence documents may be sent to TaiwanFDA directly from manufacturer.

	MPs manufacturer **& active substance of biological product**	**APIs manufacturer**
Pathways for obtaining	• **Desk-top** Inspection or NT$ 120,000~140,000 • **On-site** Inspection (since 2002) > NT$ 700,000 + travel expense	Verification the GMP Certificate issued by recognized Health Authority
Period of Validity **(Site located)**	• PIC/S member countries: 2 to 4-year cycle • Non-PIC/S member countries: 2 to 3-year cycle	According to the expiry date of the GMP Certificate submitted

Qualified Foreign Manufacturers in Taiwan

Medicinal Products

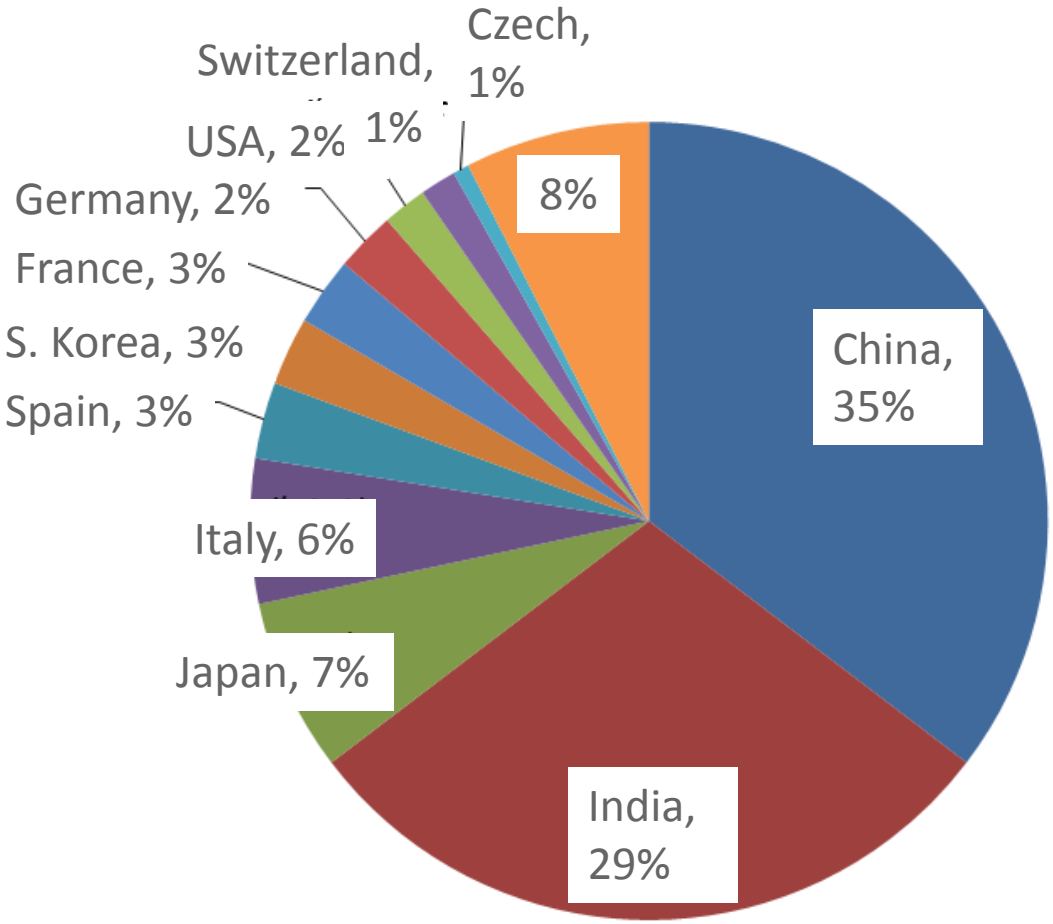


data collection until 2017.2.28

- **926** sites in total from 48 countries
- 865 sites (**93.4%**) located in PIC/S member countries
- 215 sites (**23.2%**) has been on-site inspected.

Qualified Foreign Manufacturers in Taiwan

APIs



data collection until 2017.2.28

- **614** sites in total from 36 countries
- mostly from China (217, 35%) & India (180, 29%)
- 210 sites (34.2%) located in PIC/S member countries

Outline

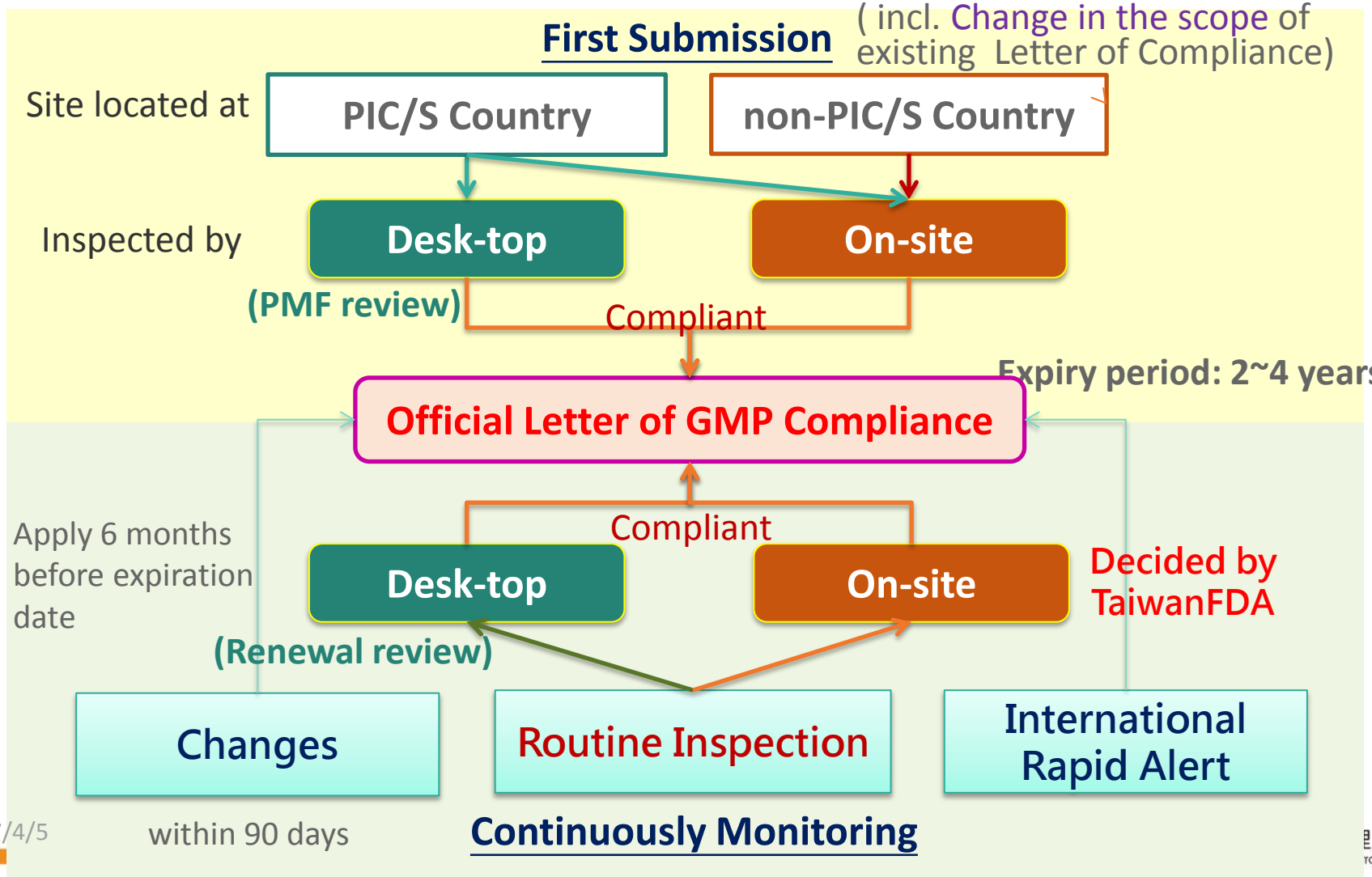
GMP Compliance of Medicinal Products in Taiwan

Process for Foreign Manufacturers

- **Issuance & Maintenance of the Official Letter of GMP compliance**
- **Application requirements**
  - **First submission (PMF review)**
  - **Renewal review**

Issuance & Maintenance of the Official Letter of GMP compliance

Desk-top inspection or On-site inspection



Application requirements

First Submission - Plant Master File (PMF) review

- Request Documentation

  ☑Application form

  ☑Site Master File (English or Chinese)

  follow the PIC/S EXPLANATORY NOTES FOR PHARMACEUTICAL MANUFACTURERS ON THE PREPARATION OF A SITE MASTER FILE (PE008-4)

  ☑Checklist of GMP Compliance & **Evidence documents [Plant Master File, PMF]**

  Where the original information is available in a language other than English or Chinese, the copy of the original information must be provide with an attestation on the accuracy of the translation.

- Application Fee
  - NT$120,000 for one dosage form/product per application;
  - NT$140,000 for maximum two dosage forms/products.

Checklist of GMP Compliance & Evidence documents

Full Package	Non-sterile	Sterile	Biological products
Part I- General information • name, address, authorised manufacturing activities, lists of products & its APIs manufactured; • any production of biological and highly sensitising, high activity, toxic or hazardous, veterinary or non-medicinal products, and the **prevention of cross-contamination** . • Dosage form(s) and process operation(s) already qualified, & be registered in this application.			
Part II – GMP Compliance (64 indicators)			
1. Quality Management System(6)	Replaced by • the most recent **inspection report** issued by its Regulatory Authority, & the CAPAs (must be applicable to the scope of the application) • List of inspection in past 3 years.	Reduced by • the most recent **inspection report** • List of inspection in past 3 years. Reduce to **34** indicators focus on the requirements of Annex 1 of PIC/S GMP Guide	As same as the full package
2. Personnel (5)			
3. Premises and Equipment (17)			
4. Documentation (2)			
5. Production (8)			
6. Quality Control (5)			
7. Outsourcing Activities (3)			
8. Complaints, Returned Products and Product Recall (3)			
9. Self Inspection (1)			
10. Distribution (1)			
11. Qualification & Validation(13)	Replaced by: • **CPP issued by reference countries**(US, UK,DE, FR, JP, BE, CA, AU, SE, EMA) • **Summary report of Validation & Declaration of Site**		

Application requirements

Renewal review

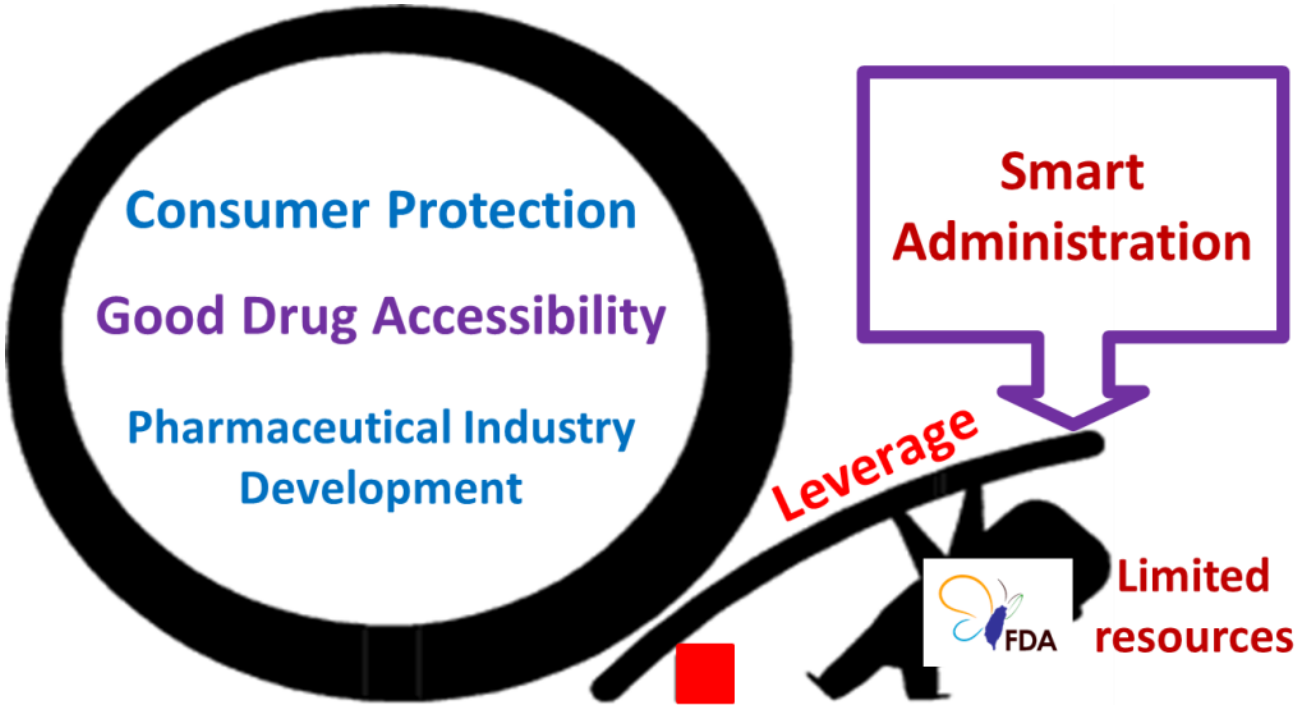
- Request Documentation
  - ☑ Application form
  - ☑ Site Master File
  - ☑ Summary reports of latest Product Quality Review
  - ☑ the most recent **inspection report** issued by its Regulatory Authority, & the CAPAs must be applicable to the scope of the application
  - ☑ Any major changes in the past 2 years
  - ☑ The periodical evaluation result of the effectiveness for the set procedures to prevent cross-contamination
- Application Fee: NT$120,000 per application

For sites located in PIC/S member countries, the inspection report may be replaced by **the current GMP Certificate**

Outline

GMP Compliance of Medicinal Products in Taiwan

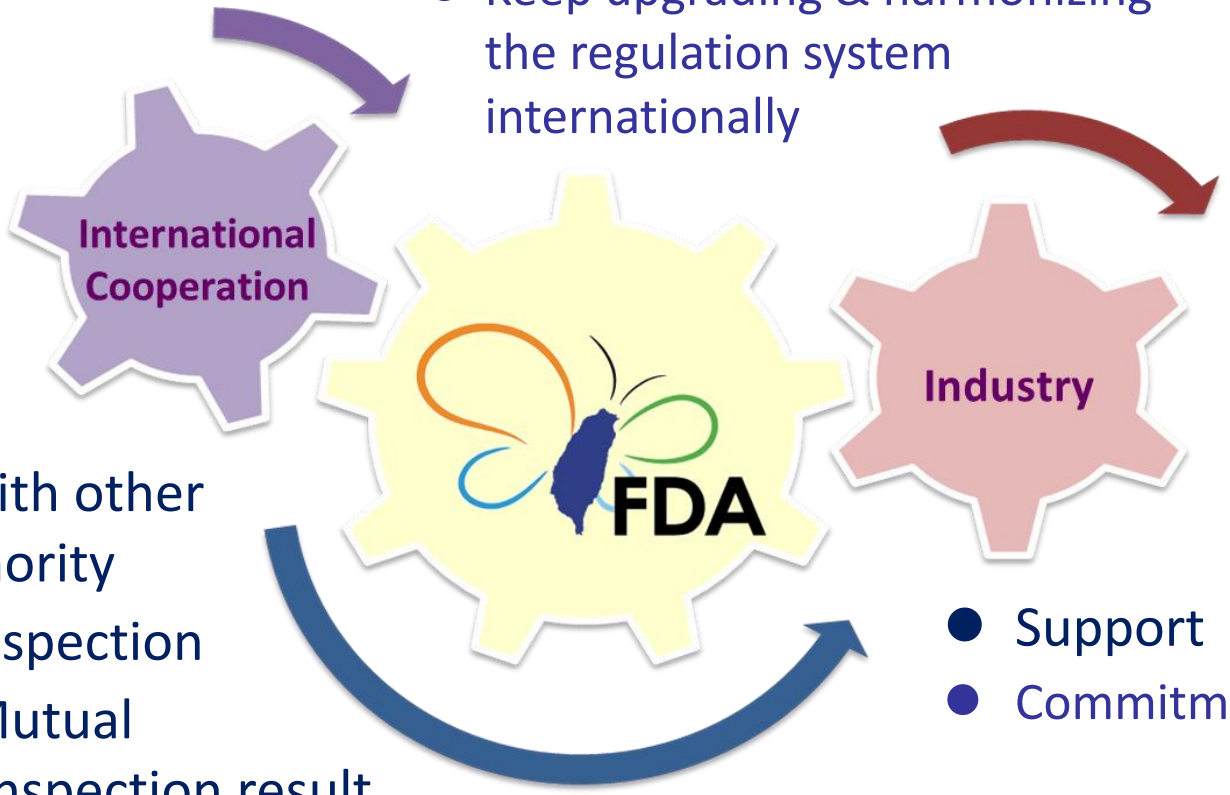
Moving Forward



Smart Administration

Leverage the resources & Work together

- Strengthen International Cooperation via PIC/S
- Networking & Trust building with other Regulatory Authority
- Conduct Joint inspection
- Agreement of Mutual Recognition of inspection result



- Keep upgrading & harmonizing the regulation system internationally
- Support
- Commitment

Thank You for Your Attention

Chiang Kai-shek Memorial Hall

Taipei 101

Yehliu Geopark

Sun Moon Lake

North-East coast of Taiwan

Pingxi Flying Lanterns

Penghu

Night Markets

Temples

For more information: Website is at http://www.fda.gov.tw