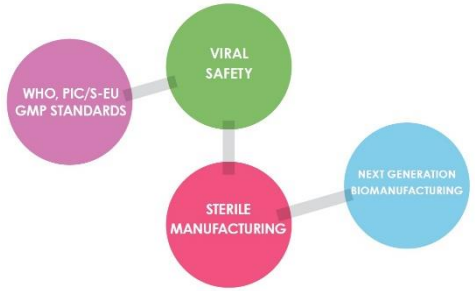


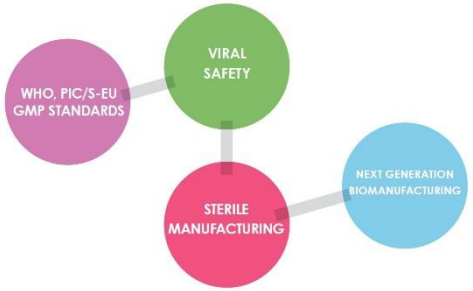
Associate Professor Chong Hock Sia, BPharm, MSc, Singapore

- Director of Quality Assurance and Senior Consultant of Audit and Licensing, Health Products Regulation Group, Singapore Health Sciences Authority
- Chair, ASEAN Joint Sectoral Committee on GMP Inspection
- Adjunct Associate Professor, National University of Singapore

GaBI Educational Workshops

18 December 2019, Hotel Gran Mahakam, Jakarta, Indonesia

2nd ASEAN Educational Workshop on
GMP FOR BIOLOGICALS/BIOSIMILARS



Current state of development of GMP for biologicals in ASEAN

Adjunct Associate Professor Chong Hock Sia, BPharm, MSc

18 December 2019

GaBi
GENERICS AND BIOSIMILARS INITIATIVE
Building trust in cost-effective treatments

PPCI
Pro Pharma Communications International

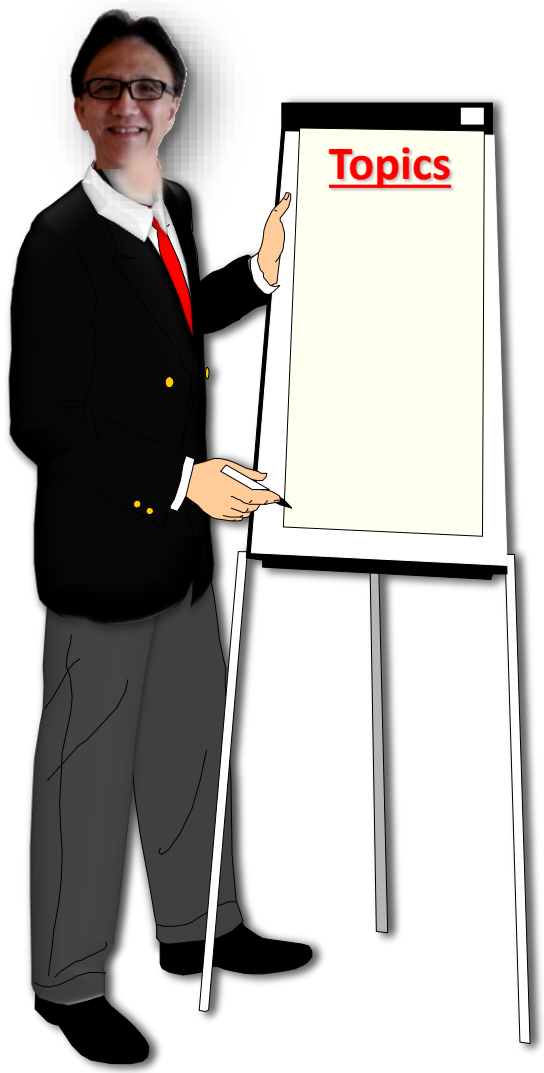
asean

2nd ASEAN Educational Workshop on GMP for Biologicals/Biosimilars

Current State of Development of GMP for Biologicals in ASEAN

Sia Chong Hock
Chair, ASEAN JSC GMP MRA

18 December 2019
Jakarta, INDONESIA



TOPICS

- **Background of ASEAN Biopharmaceuticals Market**
  - Diversity of ASEAN & Need for MRA on GMP Inspection
- **ASEAN MRA on GMP Inspection:**
  - Current Status & Expansion of Scope to include Biologicals
- **Biopharmaceutical Industry within ASEAN**
  - Specific Developments in Biologicals Manufacturing in 4 AMS
  - Singapore, Malaysia, Indonesia & Thailand
  - 4 ASEAN Listed Inspection Services
- **Conclusion:**
  - Incentives & Prospects for ASEAN Biopharmaceutical Manufacturing

Note : The terms Biologicals, Biologics & Biopharmaceuticals, used interchangeably, and includes Biosimilars

1. Background of ASEAN Biopharmaceuticals Market

ASEAN Biologicals Regulatory Framework

- To-date, review studies on biologicals regulatory framework have been done mainly in the developed world, for countries such as:

  - US, EU, Switzerland and Canada
  - Australia
  - Japan and Korea

- Few review studies have been done on the regulatory framework, including GMP inspection systems, of the Association of Southeast Asian Nations (ASEAN)

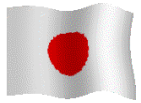
Overview of ASEAN Biopharmaceutical Industry

- Within ASEAN, the biopharmaceutical industry is generally at a nascent stage
- Vaccines are the main biopharmaceuticals manufactured due perhaps to the prevalence of infectious diseases
- In addition, there have been reports of vaccine shortages in ASEAN (from time to time) that may have prioritised manufacture of vaccines over other biopharmaceuticals
- A review of ASEAN GMP standards revealed significant differences in biopharmaceutical regulatory capacities amongst ASEAN Member States
- Such disparity can be attributed to some of the following reasons:
  - Biopharmaceuticals are currently excluded from the scope of the ASEAN Mutual Recognition Arrangement (MRA) on GMP Inspection
  - Some AMS are focusing on manufacturing pharmaceutical products, in particular generic drugs and medical devices, rather than biopharmaceuticals
  - Generally, there is great socio-political, economical and geographical diversity among the 10 AMS

Diversity of 10 AMS & Need for ASEAN Economic Community (AEC)

- **10 ASEAN Member States:**
  - Have very diverse racial, religious, socio-cultural, political, economic, trade, industry & geographical backgrounds
  - Face economic/business competition from :

 South Korea : 50 million

 Japan : 130 million

 USA : 300 million

 EU : 500 million

 India : 1.3 billion

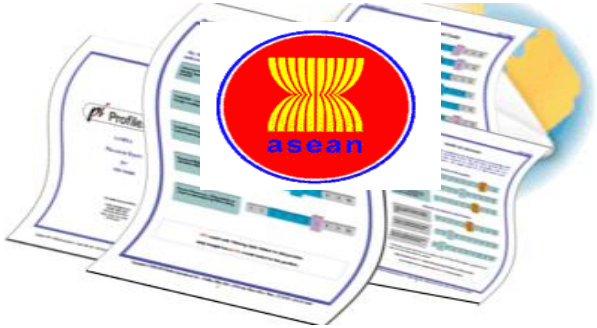
 China : 1.4 billion

- A Combined Population of 650 million people
- A Combined Economy of US$3 Trillion
- May become 4th Largest World Economy by 2030

Collective Strength can be Optimized through Creation of AEC (2015)

(2) Signing of ASEAN MRA and Formation of JSC on GMP Inspection

ASEAN Sectoral MRA on GMP Inspection



Signed by Economic Ministers of

all 10 ASEAN Member States on 10 April 2009, Pattaya, THAILAND

- PIC/S Framework Used as Basis for ASEAN MRA

- Covers Medicinal Products in Finished Dosage Forms

An ASEAN Joint Sectoral Committee (JSC) formed in 2012 to implement MRA, including creation of a Register of LIS

Register of ASEAN Listed Inspection Services (LIS)

- Singapore HSA - PIC/S Member since 1 Jan 2000

- Malaysia NPCB (now NPRA) - PIC/S Member since 1 Jan 2002

- Indonesia NADFC – PIC/S Member since 1 Jul 2012

- Thailand FDA – Applied to be 4th LIS in 2013
  Became LIS via ASEAN PoE Route (2015) &
  PICS Member with effect from 1 Aug 2016

Benefits of ASEAN MRA on GMP Inspection

(1) Avoiding duplication of GMP Audits within ASEAN

(2) Saving time, resources & costs for regulators & industry

(3) Facilitating Trade in Medicinal Products across ASEAN

(4) Quicker Access of Medicinal Products by ASEAN Patients

(5) Harmonizing ASEAN Inspection System to that of PIC/S

(6) Increased Attractiveness of ASEAN to investors from China, Japan, Korea, India, US, EU & other larger economies

Expand Scope of ASEAN MRA on GMP Inspection

Currently, scope of ASEAN MRA covers only the manufacture of *pharmaceutical products* in *finished dosage forms*

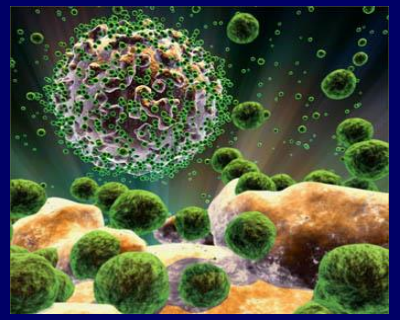


*Unlike PICS, ASEAN MRA **does NOT** currently include APIs & Biologicals*

*But, ASEAN MRA is **legally-binding***

Scope of MRA will be expanded to include:

- **Manufacture of APIs**
- **Manufacture of Biologicals**




1st ASEAN Overview Workshop on GMP for Biologicals
Da Nang, Viet Nam : 5 August 2018

Generics and Biosimilars Initiative (GaBI)

Building trust in cost-effective treatments

First ASEAN Overview Workshop on
cGMP for Biologicals/Biosimilars

Organized in collaboration with ASEAN ACCSQ-PPWG

Date: 5 August 2018, Sunday

Venue: Da Nang, Vietnam

Dear **Participants included Inspectors, Reviewers & Laboratory Analysts from 10 ASEAN Member States**

Thank you for joining the speaker faculty of the **First ASEAN Overview Workshop on cGMP for Biologicals/Biosimilars**, to be held on 5 August 2018, Sunday, in Da Nang, Vietnam. I write to follow-up with you on the preparatory works and the speaker presentation required from you for the meeting programme. As we are updating the meeting materials for participants, we would appreciate it if you can provide the required information by the indicated timeline for us to finalize the meeting programme and the programme book.

A. Meeting Programme

1. Welcome Letter from ASEAN Joint Sectoral Committee (JSC) on GMP Inspection.

We are preparing the programme book of the **First ASEAN Overview Workshop on cGMP for Biologicals/ Biosimilars**. In the programme book, we require a Welcome Letter from the ASEAN Joint Sectoral Committee (JSC) on GMP Inspection.


1st ASEAN Overview Workshop on GMP for Biologicals
SPEAKERS' FACULTY

Co-operation Initiatives between ASEAN and Korea

Annual Korea-ASEAN GMP Conferences, Meetings & Inspectors Training Courses

1ST Inspectors' Training Course : Osong, Korea 2017

Classroom Lectures

3rd Inspectors' Training Course : Seoul, Korea 2019

On-site Visits

On-Site Assessment of FDA Philippines

FDA Philippines will be recommended for inclusion as 5th ASEAN LIS at 28th ASEAN PPWG Meeting

Article 6 : ASEAN Sectoral MRA on GMP Inspection

2. The JSC shall be responsible for:

(a) listing, verification and termination of Inspection Services in accordance with this Sectoral MRA;

(b) providing a forum for discussion of issues that may arise concerning the implementation of this Sectoral MRA;

(c) the formation of the Panel of Experts and the appointment of independent experts. An independent expert shall not be a member of the Panel of Experts, and shall only be engaged when necessary;

(d) reviewing and proposing amendments to the scope and coverage of this Sectoral MRA; and

(e) considering any other matters and taking appropriate technical decisions relating to the implementation of this Sectoral MRA.

Expansion of scope to include biologicals will be on the Meeting Agenda of forthcoming JSC GMP MRA Meetings!

3. Biopharmaceutical Industry within ASEAN

Specific Developments in Biologicals Manufacturing in 4 AMS : SG, MY, ID & TH

- Singapore does NOT have its own biopharmaceutical manufacturing industry
- However, it is one of the leading locations for MNC biopharmaceutical manufacturing plants, where innovative products are launched and produced
- Industry leaders like Pfizer, Novartis, Sanofi, AbbVie and Amgen have global manufacturing hubs in Singapore for a wide range of products including biologics
- For example, Amgen's decision to pick Singapore for its 1st manufacturing facility in Asia is due to its biopharmaceutical infrastructural capabilities, continuous government commitment to biotech manufacturing and its skilled workforce
- Today, >6,000 people in the skilled workforce are employed in the biopharmaceutical sector, more than 2X the number since early 2000s

3. Biopharmaceutical Industry within ASEAN ….. Cont'd

Singapore Malaysian, Indonesia & Thailand …… Cont'd

- The focus in Malaysia & Indonesia is still on the generic pharmaceutical manufacturing industry
- However, in Indonesia, the domestic demand for biologics such as vaccines has started a drive for biopharmaceutical manufacturing industry in recent years
- The Indonesian government has mandated that the industry should support the technology for biopharmaceutical products to reduce reliance on external sources
- Several companies have taken up this challenge and have invested considerable sums in product & manufacturing licenses, facilities and training
- An example is PT Kalbio Global Medika in Jakarta. This facility has been built with state-of-the-art technology, and has earned an honorable mention in the 2017 ISPE FOYA Awards

Singapore Malaysian, Indonesia & Thailand ….. Cont'd

Biopharmaceutical market size in Thailand is USD 1 billion

Local biopharma manufacturers include:

- **GPO – supported by Merieux Biologicals Products:**
  – Influenza Vaccine, Japanese Encephalitis Vaccine, Rabies Vaccine & Hepatitis B Vaccine
- **Thai Red Cross:**
  Vaccines (BCG, Rabies Vaccines) and Blood Products (Albumin, IVIG, Factor VIII)
  – only plasma fractionation centre in ASEAN
- **Bionet-Asia:**
  Private vaccine company with focus on technological innovation, including genetic engineering, cell culture & vaccine formulation
- **ATMP Facilities – CTGTP & CAR T Cells**
- **GPO: Upgraded Facilities will begin Production of MABs**

Biosimilars – Some Background & Development

Bright Prospects for Biosimilar Manufacturing in ASEAN

- **1st Biosimilar approved by US FDA is *Zarxio (Sandoz)* containing filgrastim Zarxio is the biosimilar of the innovator product - *Neupogen™ (Amgen)***
- Neupogen™ was approved in **1991** while Zarxio was only approved in **2015**
- **As at end 2018, only 9 Biosimilars had been approved by US FDA**
- **Price of a Biosimilar is estimated to be 65% to 85% of Innovator Product; Due to Lower R&D/Regulatory Costs**
- **Global Market for Biosimilars expected to reach US$ 35 billion by 2020, driven by patent expiry of up to 10 top-selling innovator products!**
- **More approvals of Biosimilars by the US FDA and EMA can be expected**
- **ASEAN should consider investment in the biopharmaceutical industry, including biosimilars market. There appears to be very bright prospects!**

4. Conclusion

Incentives for ASEAN Biopharmaceutical Manufacturing

- ASEAN governments are providing numerous incentives to investments by global biopharmaceutical manufacturers
- To begin with, the lower manufacturing costs in some AMS can enable greater cost-savings in the manufacture of biosimilars
- In addition, ASEAN is experiencing a general epidemiological shift from communicable acute to non-communicable chronic diseases, and biopharmaceuticals may play an increasing role in managing the latter
- With a combined population of 650 million, the ASEAN market may provide a sizeable patient population that attracts the importation and manufacturing of biopharmaceuticals into the region
- Thus, there is a need to ensure that its regulations, including GMP framework, is adequate in assuring the quality of biopharmaceuticals


THANK YOU