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REGULATORY REQUIREMENTS FOR REGISTRATION OF DRUGS IN ASEAN COUNTRIES

J. Sai Bhavana*, M. Venkata Sowmya, Brahmaiah Bonthagarala, G. Ramakrishna, M. V. Nagabhushanam and D. Nagarjuna Reddy

Department of Pharmaceutical Management and Regulatory Affairs, Hindu College of Pharmacy, Amaravathi Road, Guntur, Andhra Pradesh, India-522002.

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***Corresponding Author**
J. Sai Bhavana
Department of Pharmaceutical Management and Regulatory Affairs, Hindu College of Pharmacy, Amaravathi Road, Guntur, Andhra Pradesh, India-522002.

ABSTRACT

The ASEAN region is emerging in the pharmaceutical marketplace with several countries leading in quality, efficacy, safety, BE/BA, and variations. It is important for the region to have more ASEAN countries accredited to PIC/S for the implementation and maintenance of harmonized cGMP standards and quality systems. In the author's experience, it would be good to have common filing procedures with full mutual acceptability in the ASEAN region. This will ensure rapid patient access to drugs, such as seen in the EU with Mutual Recognition Procedure (MRP), Decentralized Procedure (DCP) and Centralized Procedure (CP). Economic diversity, language, uneven distribution of wealth, intellectual property, and lack of harmonization of guidelines and their implementation are some of the challenges currently creating hurdles for pharmaceutical companies looking to penetrate these regions more effectively.

KEYWORDS: ASEAN Countries, Mutual Recognition Procedure (MRP), Decentralized Procedure (DCP) and Centralized Procedure (CP).

1. INTRODUCTION

Association of Southeast Asian Nations (ASEAN) was founded on August 8, 1967. The Foreign Ministers of Indonesia, Malaysia, the Philippines, Singapore and Thailand – sat down together in the main hall of the Department of Foreign Affairs building in Bangkok, Thailand and signed a document. By virtue of that document, the Association of Southeast Asian Nations (ASEAN) was born**.** The five Foreign Ministers who signed it – Adam Malik

of Indonesia, Narciso R. Ramos of the Philippines, Tun Abdul Razak of Malaysia, S. Rajaratnam of Singapore, and Thanat Khoman of Thailand – would subsequently be hailed as the Founding Fathers of probably the most successful inter-governmental organization in the developing world today. And the document that they signed would be known as the ASEAN Declaration. ASEAN is a regional grouping that promotes economic, political, and security cooperation among its ten members: Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam. In 1976, the members signed the Treaty of Amity and Cooperation, emphasizing ASEAN's promotion of peace, friendship, and cooperation to build solidarity. Today, ASEAN is considered one of the most successful intergovernmental organizations in the developing world. Since its founding, the grouping has expanded to include other Southeast Asian states – Brunei (1984), Vietnam (1995), Laos (1997), Myanmar (1997) and Cambodia (1999).[1]

Some of the joint development programs first undertaken by ASEAN include projects to[2-3]**:**

- increase food production
- promote tourism
- ease travel restrictions, and
- enhance cooperation in the field of mass media through exchanges of radio and television programs.
- Plans were also put in place to liberalize trade among members in a bid to improve intraregional trade.

SIGNIFICANCE OF ASEAN LOGO

Fig. 1: ASEAN Countries Logo.

- The Emblem of the Association of Southeast Asian Nations is the emblem of ASEAN adopted in July 1997 together with the ASEAN flag.

- Although the current emblem was already in use for years, the official guidelines were adopted at the 6th Meeting of the ASEAN Coordinating Council (ACC) in Hanoi, 8 April 2010.
- The ASEAN Emblem represents a stable, peaceful, united and dynamic ASEAN. The colors of the Emblem — blue, red, white and yellow — represent the main colors of the state crests of all the ASEAN Member States.
- The blue represents peace and stability. Red depicts courage and dynamism, white shows purity and yellow symbolizes prosperity.
- The stalks of padi in the centre of the Emblem represent the dream of ASEAN's Founding Fathers for an ASEAN comprising all the countries in Southeast Asia, bound together in friendship and solidarity.[2]
- The circle represents the unity of ASEAN.
- The ten bound stalks of rice in the centre of the Emblem represent the member states of ASEAN. They represent the dream of ASEAN's Founding Fathers for an ASEAN comprising all the countries in Southeast Asia, bound together in friendship and solidarity.

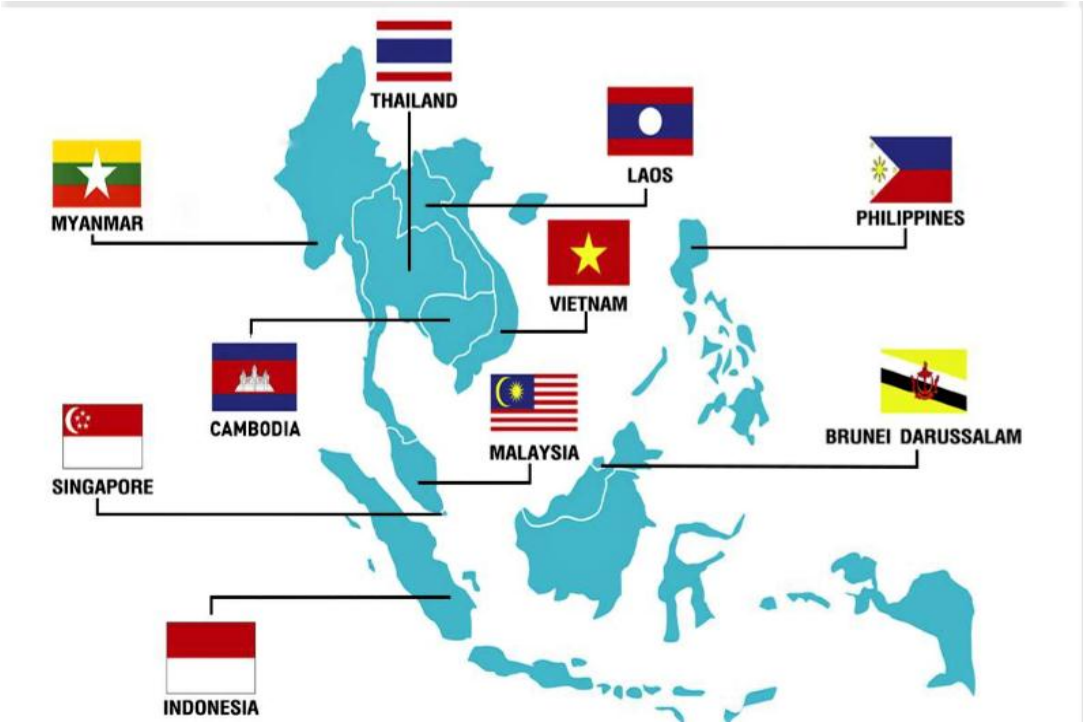

Fig. 2: Different ASEAN Countries.

2. AIMS AND PURPOSES

As set out in the ASEAN Declaration, the aims and purposes of ASEAN are:

- To accelerate the economic growth, social progress and cultural development in the region through joint endeavors in the spirit of equality and partnership in order to strengthen the foundation for a prosperous and peaceful community of Southeast Asian Nations.[3]
- To promote regional peace and stability through abiding respect for justice and the rule of law in the relationship among countries of the region and adherence to the principles of the United Nations Charter.
- To promote active collaboration and mutual assistance on matters of common interest in the economic, social, cultural, technical, scientific and administrative fields.
- To provide assistance to each other in the form of training and research facilities in the educational, professional, technical and administrative spheres.
- To collaborate more effectively for the greater utilization of their agriculture and industries, the expansion of their trade, including the study of the problems of international commodity trade, the improvement of their transportation and communications facilities and the raising of the living standards of their peoples.
- To promote Southeast Asian studies; and to maintain close and beneficial cooperation with existing international and regional organizations with similar aims and purposes, and explore all avenues for even closer cooperation among themselves.

FUNDAMENTAL PRINCIPLES[4]

In their relations with one another, the ASEAN Member States have adopted the following fundamental principles, as contained in the Treaty of Amity and Cooperation in Southeast Asia (TAC) of 1976:

- Mutual respect for the independence, sovereignty, equality, territorial integrity, and national identity of all nations.
- The right of every State to lead its national existence free from external interference, subversion or coercion.
- Non-interference in the internal affairs of one another; Settlement of differences or disputes by peaceful manner.
- Renunciation of the threat or use of force; and Effective cooperation among themselves.[4]

ORIGIN

The ASEAN Consultative Committee for Standards & Quality was formed to facilitate & complement the ASEAN Free Trade Area (AFTA).

Efforts toward harmonization of ASEAN pharmaceutical regulations were initiated through the ACCSQ & it leads to formation of Pharmaceutical Product Working Group.

OBJECTIVE

The main objective of ASEAN is to accelerate the economic growth, social progress and cultural development among its members & protection of regional peace and stability.

To develop harmonization schemes of pharmaceutical regulations, to eliminate technical barriers to trade posed by these regulations without compromising on drug quality, safety and efficacy.

3. DRUG REGISTRATION[5]

Permission granted by the relevant state authority to use and distribute a certain drugs;

Main aim of registration is to ensure that the users get only safe, effective drugs of high quality.

ASEAN COUNTRIES

Brunei	Cambodia
Indonesia	Lao People's Democratic Republic
Malaysia	Myanmar
Philippines	Singapore
Thailand	Vietnam

MAJOR EXPORTS

- Guar gum
- Menthol
- Chawanprash
- Herbal extracts etc

4. FORMAT FOR DRUG REGISTRATION[6-9]

ACTD - Common Technical Dossier

Common application format that will be submitted to ASEAN regulatory authorities for the registration of pharmaceutical products for human use.

Even though some of the Individual ASEAN Countries have their own drug registration formats, all ASEAN countries accept the ACTD. Countries like Brunei Darussalam,

Cambodia, Myanmar, Thailand, does not have any separate drug registration format but follow ACTD.

BRUNEI DARUSSALAM

There is separate cell for Pharmaceutical services and the Department of Pharmaceutical service is mainly responsible for executing the control of drugs. There are more than 3500 Pharmaceutical products are registered. For the registration of Pharmaceutical products one has to submit the detailed monograph of the said product giving the details of the product pertaining to its Pharmacology, Pharmacokinetics, Toxicology, Biopharmaceutics, Clinical Pharmacology, Clinical efficacy, Safety etc. as required for CTD and any other supporting documents like Clinical trial, comparative studies.

CAMBODIA

National policy on TM/CAM was issued in 1996 and regulations were issued in 1998. Regulation of herbal medicines in Cambodia was introduced in 1998. Herbal medicines are regulated as over-the-counter medicines and for self-medication only.

Cambodia follows the common ASEAN CTD for registration of Pharmaceutical Product for Human use. There are more than 48 registered herbal medicines; however, none of them are included on National essential drug list. Herbal medicines in Cambodia are sold in pharmacies as over-the-counter medicines, in special outlets, by licensed practitioners and without restriction.[5]

INDONESIA

"National Policy on Development of Traditional Medicine" was issued in 2000. Laws and regulations on TM/CAM were first issued in 1993. Through a separate law for herbal medicines, regulation was established in 1993, and updated in 1994 and 1995. Herbal medicines are regulated as over-the-counter medicines, as a separate regulatory category and as traditional medicines. There are approx. 8632 registered herbal medicines in Indonesia. No herbal medicines are included on a National essential drug list. Herbal medicines are sold in pharmacies as over-the-counter medicines, in special outlets, by licensed practitioners and without restriction. Indonesia has its own drug registration format and also follows ASEAN CTD.

LAO PEOPLE'S DEMOCRATIC REPUBLIC

National policy on TM/CAM was included in the National Drug Policy issued in 1998. Regulations on herbal medicine in the Lao People's Democratic Republic were issued in 2002; Herbal medicines are regulated as over-the-counter medicines. In the Lao People's Democratic Republic herbal medicines are sold in pharmacies as over-the-counter medicines and by licensed practitioners. Lao PDR has its own has drug registration format and also follows ASEAN CTD.

MALAYSIA

National policy on TM/CAM, which was launched in the year 2001. The registration and licensing of TM/CAM is legislated through the Control of Drugs and Cosmetics Regulations 1984. Regulation for traditional medicines, including herbal medicines and dietary supplements formed part of the Control of Drugs and Cosmetics Regulations in 1984. Traditional medicines are allowed to be sold as over-the-counter medicines. As of December 2003, approximately 1200 traditional medicines, including herbal products are registered and regulated by DCA. However, none of these products are included on the National essential drug list. In Malaysia, herbal medicines are sold in pharmacies as over-the-counter drugs without any restrictions. For registering Pharmaceutical product on-line drug registration facility is available.

MYANMAR

National policy on TM/CAM was issued in 1993. Myanmar follows the common ASEAN CTD for the registration of Pharmaceutical Products for human use. There are approx 3,678 registered traditional medicines in Myanmar. In Myanmar, the Traditional Medicines Drug law was enacted in 1996 to ensure the quality, safety and efficacy of traditional medicines. The regulatory statues used for herbal medicine are over-the-counter medicines and herbal medicine as a separate category. Herbal medicines are sold in pharmacies as over-the-counter medicines and without restriction.[6]

PHILIPPINES

National policy on TM/CAM was issued in 1997. The regulations on herbal medicines were issued in 1984; these regulations are separate form those for conventional pharmaceuticals. Herbal medicines are regulated as over-the-counter medicines. The Philippines has separate registration system for herbal medicines; however, the number of registered herbal medicines is not available. In the Philippines, herbal medicines are sold in pharmacies as over-the-

counter medicines and in special outlets. Philippines has its own drug registration formats and also follows ASEAN CTD.

SINGAPORE

National policy on TM/CAM was issued in 1995. There are National regulations on herbal medicines in Singapore. Herbal medicine is regulated as over-the-counter medicines. Singapore has its own drug registration format and follows common ASEAN CTD. There are no restrictions on the sale of herbal medicines, as long as they comply with the National regulations.

VIETNAM

National policy on TM/CAM is currently being developed. Laws and regulations on TM/CAM were issued in 1989. Herbal medicines are regulated as prescription and over-the-counter medicines. Vietnam has its own drug registration format and also follows ASEAN CTD. There are approx. 1573 registered herbal medicines in Vietnam; 267 herbal medicines are included on the National essential medicines list of 1996. In Vietnam, herbal medicines are sold in pharmacies as prescription and over-the-counter medicines, in special outlets and by licensed practitioners.[7]

THAILAND

The National policy and programme on traditional medicine was issued in 1993, when the Institute of Thai Traditional Medicine was officially established under the Department of Medical Services. National laws and regulations on traditional medicines were issued in 1967 under the Drug Act B.E. 2510, which is divided into two parts covering modern and traditional medicines. Registered traditional medicines can be divided into prescription medicines or over-the-counter medicines. Medical, health and structure/function claims may be made about herbal medicines. Thailand has its own drug registration format and also follows ASEAN CTD. There are more than 2000 herbal medicines registered in Thailand; a total of more about 20 herbal preparations are included in the National list of essential drugs, A.D. 1999. Herbal medicines are sold in pharmacies as over-the-counter drugs, or licensed practitioners may make their own herbal preparations and sell them to patients. For registered household herbal medicines, there are no restrictions on sales.

Table 1: Regulatory Framework In Asean Region.

Country	Regulatory body	Time line
Singapore	HSA	90 – 240 working days
Malaysia	NPCB	80 – 210 working days
Philippines	FDA	6 months
Myanmar	Department of FDA	1 year
Thailand	TFDA	70 to 110 working days
Cambodia	Department of Drugs & food	1 year
Indonesia	NADFC	100 – 150 working days
Vietnam	MOH	1 year

5. ASEAN COMMON TECHNICAL DOSSIER AND ITS GUIDELINES[10-14]

This guideline merely demonstrates an appropriate write-up format for acquired data. However, applicants can modify, if needed, to provide the best possible presentation of the technical information, in order to facilitate the understanding and evaluation of the results upon pharmaceutical registration. Throughout the ACTD, the display of Information should be unambiguous and transparent, in order to facilitate the review of the basic data and to help a reviewer become quickly oriented to the application contents. Text and tables should be prepared using margins that allow the document to be printed on either A4 or 8.5 x 11 paper.

The left-hand margin should be sufficiently large that information is not obscured by the method of binding. Font and size, (Times New Roman, 12-point font), for text and tables should be of a style andsize that are large enough to be easily legible, even after photocopying. Every page should be numbered, with the first page of each part designated as page 1. For a paper, Common Technical Acronyms and abbreviations should be defined the first time they are used In each part.[8]

GUIDELINES

Part I: Table of Content Administrative Information and Prescribing Information

Section A: Introduction

Section B: Overall ASEAN Common Technical Dossier Table of Contents

Section C: Documents required for registration (for example, application forms, labelling, Product Data Sheet, prescribing information)

Part II: Quality Document

Section A: Table of Contents

Section B: Quality Overall Summary

Section C: Body of Data

Part III: Nonclinical Document

Section A: Table of Contents

Section B: Nonclinical Overview

Section C: Nonclinical Written and Tabulated Summaries

1. Table of Contents
2. Pharmacology
3. Pharmacokinetics
4. Toxicology

Section D: Nonclinical Study Reports

1. Table of Contents
2. Pharmacology
3. Pharmacokinetics
4. Toxicology

Part IV: Clinical Document

Section A: Table of Contents

Section B: Clinical Overview

Section C: Clinical Summary

1. Summary of Biopharmaceutics and Associated Analytical Methods
2. Summary of Clinical Pharmacology Studies
3. Summary of Clinical Efficacy
4. Summary of Clinical Safety

5. Synopses of Individual Studies

Section D: Tabular Listing of All Clinical Studies

Section E: Clinical Study Reports

Section F: List of Key Literature References.[9]

6. CONCLUSION

The ASEAN region is emerging in the pharmaceutical marketplace with several countries leading in quality, efficacy, safety, BE/BA, and variations. It is important for the region to have more ASEAN countries accredited to PIC/S for the implementation and maintenance of harmonized cGMP standards and quality systems. In the author's experience, it would be good to have common filing procedures with full mutual acceptability in the ASEAN region. This will ensure rapid patient access to drugs, such as seen in the EU with Mutual Recognition Procedure (MRP), Decentralized Procedure (DCP) and Centralized Procedure (CP). Economic diversity, language, uneven distribution of wealth, intellectual property, and lack of harmonization of guidelines and their implementation are some of the challenges currently creating hurdles for pharmaceutical companies looking to penetrate these regions more effectively.

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