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Harmonization Of Regulatory Requirements For Registration Of Drug Products In Asean Nations.

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ABSTRACT

ASEAN is the union of ten South East Asian nations, which was formed in the year 1967, with the objective to promote Pan- Asianism and intergovernmental cooperation and facilitates economic, political, military, educational and socio- cultural integration amongst its members and other Asian countries. Harmonization of Pharmaceutical Standards all began in 1997, with the objective to develop a Harmonized scheme of Pharmaceutical regulation and to eliminate technical barriers to trade, however ensuring those pharmaceutical products penetrating the ASEAN markets are of safe, efficacious and of quality, when the 13thACCSQ meeting in March 1997 saw the need to establish a Pharmaceutical Product Working Group. Even though the Harmonization process took place in 1997, because of the differences in the regulatory requirements between different ASEAN nations, causing in the delay of drug product approval, which resulted in the delayed access of medicines to the people. The objective is to study the extent of possible Harmonization between ASEAN nations, with the revised and updated Harmonized guidelines, the differences between the regulatory requirements between different countries for product approval can be reduced which ultimately can lead in faster approval and early access to safe and quality medicines to the people.

Keywords: ACCSQ, ASEAN, PPWG, ASEC

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INTRODUCTION

ASEAN – Association of South East Asian Nations, is a regional intergovernmental organizationcomprising ten Southeast Asian states which promotes Pan-Asianism and intergovernmental cooperation and facilitates economic, political, military, educational and cultural integration amongst its members and Asian states. Since its formation on 8 August 1967 by Indonesia and its members. The organization's membership has expanded to include Brunei, Cambodia, Laos, Myanmar, and Vietnam[1]

The countries under consideration include

- ✓ Malaysia
- ✓ Singapore
- ✓ Thailand
- ✓ Philippines
- ✓ Vietnam

Figure 1: ASEAN Nations

Need for Harmonization

ASEAN, which comprises of 10 nations, if the drug registration requirements vary from one country to another, which may delay drug approval process, further resulting in the delayed access to safe, efficacious and quality medicines to the people. From the industry perspective, there will be duplication of data, irrational use of resources and time as filing to be done individually for all the 10 nations. If the drug registration requirements are harmonized, it will result in the fast approval and early access to medicines and will save the resources and time of industry and regulatory authorities.

The main objective of the work is to evaluate the extent of harmonization of regulatory requirements for registration of drug products in between ASEAN countries.

- ✓ Understanding the regulatory requirements for drug product registration in between different ASEAN nations
- ✓ Clearly demarcating the differences in the regulatory requirements for drug product registration in between ASEAN nations
- ✓ To propose a Unified Harmonization Plan where it can reduce the drug product registration time in between ASEAN nations and results in better Harmonization.

DISCUSSION

Harmonization process of ASEAN nations

Harmonization of Pharmaceuticals Standards all began in 1997, when the 13thACCSQ (ASEAN Consultative Committee on Standards and Quality) meeting in March 1997 saw the need to establish a Pharmaceutical Product Working Group. A proposal was set up by Malaysia, which was an endorsed by the

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relevant bodies. Accordingly PPWG (Pharmaceutical product working group) had its first meeting in Sept 1999 with Malaysia as(Chair) and Thailand as (Co-Chair)[2]

Objectives of PPWG (Pharmaceutical product working group)

- To develop a Harmonization scheme of Pharmaceutical Regulation.
- To eliminate technical barriers to trade, however ensuring those pharmaceutical products penetrating the ASEAN markets are safe, efficacious and of quality[2]

Organizational structure of PPWG[2]

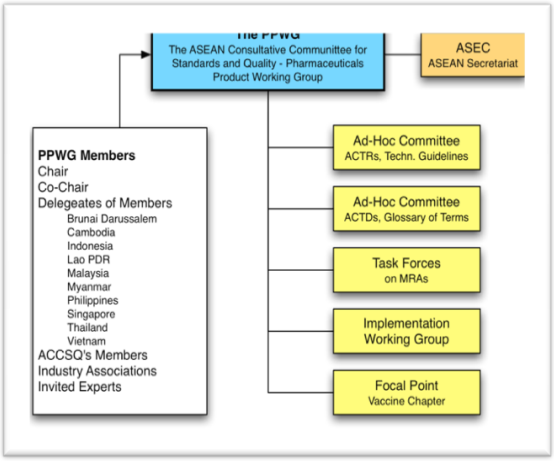

Figure 2: Organizational structure of PPWG meetings

Description

- All PPWG meetings are convened by the chair of the PPWG, or in his absence by his co-chair. There are usually one or two PPWG meetings per year. At the end of each PPWG meeting it is determined the date and country in charge for organising the next venue of the next meeting.
- PPWG members include delegates from ASEAN nations, ACCSQ's members, industry associations, invited experts.
- The PPWG is headed by ASEC (ASEAN Secretariat)
- The PPWG constitutes Ad-Hoc Committees related to ACTD's ACTR's guidelines, it also constitutes Task forces on Mutual Recognition Agreements and Working groups for the implementation of guidelines.

PPWG Consultation procedure[2]

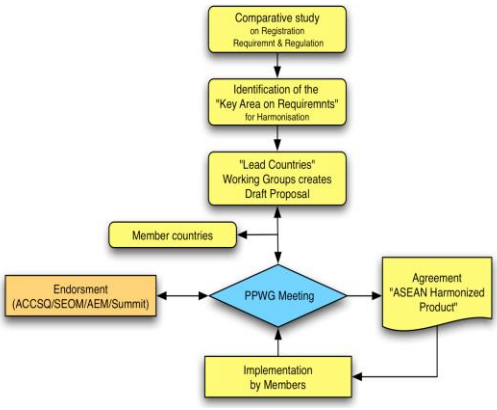

Figure 3: PPWG Consultation procedure

Description

The first step is to exchange and review information on the existing pharmaceutical requirements and regulations among ASEAN member countries. The next step is to conduct comparative studies, between ASEAN regulations and other international accepted standards.

Following surveys and comparative studies the ASEANs 'Key areas' for harmonisation are identified

- The PPWG assigns a 'Lead Country' and 'ad hoc' or 'permanent' working groups that should set up to discuss scientific and technical aspects of each harmonisation topic. These working groups shall prepare a draft proposal of how to harmonise the identified key area. As there are various international guidance documents, ASEAN has to determine which of these are applicable for the ASEAN region. If there is no existing international guidance or in case the international guidance is not applicable for ASEAN, the region will develop their own. The working groups are in open dialogue with industry representatives and experts from international organisations.
- The lead country of the working groups presents the draft proposals for harmonisation of a specific key area at the PPWG meeting for discussion and agreement. If there are objections the draft and successive revisions are circulated for comments to the individual ASEAN health authorities who send it to their respective national industry association. The lead country is tasked to revise the draft proposals, taking into account comments received from health authorities and industries. Once consensus is reached the final draft is agreed by regulators of ASEAN at the PPWG meetings. Agreements are made upon common consensus of all member states. Often Myanmar delegates could not attend the PPWG meetings, in this case they send their position by post-mail
- Ratification: Once PPWG agreed on the final draft, it is channelled to the appropriate higher bodies for endorsement or decision.
- These harmonisations decisions are implemented within clear set timelines. Implementation follows according to the respective national procedures and the implementation is monitored by the respective lead country of the working group. PPWG reports their achievements back to the ACCSQ. At all PPWQ meetings a delegate from the ASEAN secretariat is present to channel and make connection to other ASEAN bodies. New regulatory ASEAN guidelines should be published on the ASEAN-Secretariat's homepage and on each individual health authority's homepage.
- Implementation goes along with Training, Support and Assessment. PPWG organises various trainings for regulators and industry with support from international organisations. On the other hand, there are intra-ASEAN trainings, where more developed ASEAN countries train others, e.g. twinning system between CVML and ASEAN-6 countries. PPWG networks with various international organisations and regulators from other regions, (e.g. WHO, ICHGCG, APEC) in order to working towards adopting a harmonised best practice approach for ASEAN. They seek funding and training from cooperation projects with its international dialogue partners[2]

Outcomes of Harmonization[2]

At the first PPWG meeting, the Terms of Reference were agreed and it was decided that the topics selected for harmonization would be divided into Safety, Quality and Efficacy to reflect the three criteria which are the basis for approving medicinal products. One of the PPWGs key topic is the idea of an 'ASEAN pharmaceutical product'. This means that same regulatory requirements apply for the registration of a medicinal product among the ASEAN member countries.

ACTD

It gives information on the format and structure of the dossier that shall be commonly used for applications in the ASEAN region. The ACTD should serve as a locator for documentation that has been compiled for a marketing authorisation application. It does not give any recommendations on the actual content of the dossier.

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ACTR

The ACTR (ASEAN Common Technical Regulations) is as set of written material intended to guide applicants to prepare an application in a way that is consistent with the expectations of all ASEAN Drug Regulatory Authorities. It is guidance for the preparation of the ACTD.

ACTD Check lists

The ACTD check-lists give recommendations to which extend documentation has to be provided for the different product classifications. The different ASEAN product classifications are namely a New Chemical Entity, Biotechnology derived products, Major/ Minor Variations or Generic Products. Until now these classifications are not clearly defined. The applicant therefore has to apply the regulations of each national regulatory authority and consult them for advice, e.g. pre-submission meetings.

Table 1: Comparison Of Drug Registration Requirements In Between Asean Countries[3]

Country	Dossier Format	Registration Fee	Renewal Fee	Retention Fee	Product Registration Validity
Malaysia	ACTD	2200 MR- single API	1000 MR		5 years
Singapore	ACTD/CTD	4400 SD		300 SD	5 years
Thailand	ACTD	2000 TB			Life time (need to commercialize at least once in every 2 years to retain registration
Philippines	ACTD	1052 US$	1000 US$		5 years
Vietnam	ACTD	4,500,000 VD	4,500,000 VD		5 years

MR – Malaysian Ringgit, SD – Singapore Dollars, TB – Thai Bhat, VD – Vietnamese Dong

ASEAN Quality guidelines

The majority of pharmaceutical products reviewed by ASEAN Drug Regulatory Authorities are generics. For generic applications especially the quality (Part II ACTD) is of importance as non-clinical (Part III) and clinical (Part IV) do not need to be submitted. Therefore PPWG has reviewed available international guidelines and determined which ones were applicable for ASEAN. Four 'ASEAN ACTR-Quality Guidelines' were developed to set standards and provide guidance especially for local generic manufacturers. The existing international guidelines are more or less transposed into simplified ASEAN guidelines with the exception of the ASEAN stability guideline.

Table 2: Administrative Documents Requirements In Between Asean Counsatries [3]

Country	License	Good Manufacturing Practice certificate	Free Sale Certificate	Certificate of Pharmaceutical Product
Malaysia	Not required	Required (Notary)	Required (Notary)	Common original
Singapore	Not required	Required (Notary)	Required (Notary)	Common original
Thailand	Required (Notary)	Required (Notary)	Not required	Country specific
Philippines	Required (Notary)	Required (Notary)	Not required	Country specific
Vietnam	Required (Notary)	Required (Notary)	Not required	Country specific (Legalized)

The ACTD and ACTR clearly indicates that for NCE and Biotechnological Products the ICH reference guidelines should be followed. For Generics and Variations the respective ASEAN Guidelines can apply[2]

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ANALYTICAL VALIDATION GUIDELINE

'The ASEAN Guideline for Validation of Analytical Procedures', developed with Thailand as lead country was adopted in 2003. This ASEAN guideline mainly incorporated the two ICH Guidelines Q2A 'Validation of Analytical Methods Definition and Terms' and ICH Q2B 'Validation of Analytical Procedure Methodology' which are today known as Q2(R1). The objective of this guideline is to guide industry to demonstrate that an analytical procedure is suitable for its intended purpose[2]

Table 3: Audit Requirements In Between Asean Countries [3]

Country	Finished product Audit Requirements	API Audit Requirements	Audit Fee	Drug Master File
Malaysia	Required	Not Required	25000 MR	Closed Part DMF to RA
Singapore	PIC Audit	PIC Audit	Not Required	Closed Part DMF to RA
Thailand	PIC Audit	Not Required	Not Required	Open Part of DMF
Philippines	Plant Registration	Not Required	200 USD	Open Part of DMF
Vietnam	PIC Audit	Not Required	Not Required	Open Part of DMF

BA/BE Studies Guideline

The ASEAN Guideline for the conduct of Bioavailability and Bioequivalence studies was developed with Malaysia as lead country and adopted in 2004.

The ASEAN guideline took the definition of essential similar products from the former EU NTA 1998. Thereafter a medicinal product is essential similar to an originator product if it contains the quantity and quality of active substance and the same pharmaceutical form. For immediate release products, the concept of essential similar applies also to different oral forms e.g. tablets and capsules with the same drug substance. An important difference to the EU Guidance was, that ASEAN did not adapt the definition that essential similar medicinal products should have the same quantitative and qualitative composition in terms of excipients

ASEAN require for an innovator product the full clinical dossier including clinical and non-clinical has to be submitted. A reference product used in BE studies must be an innovator product.

In order to broaden this restriction ASEAN added that 'if the innovator product is not available in the country, an alternative comparator product approved by drug regulatory authorities of the respective country can be used[2]

Table 4: Stability And Sample Requirements In Between Asean Countries [3]

Country	Stability condition	Minimum stability requirement at the time of filing	Sample Requirements	Sample Validity Requirement
Malaysia	30/75	12Months /3Batches	Not Required	Not Required
Singapore	30/75	12Months /3Batches	Not Required	Not Required
Thailand	30/75	12Months /3Batches	6 Packs	12 Months
Philippines	30/75	12Months /3Batches	6 Packs	12 Months
Vietnam	30/75	12Months /3Batches	Not Required	Not Required

Stability Study Guidelines

This guideline was developed with Indonesia as lead country and adopted in July 2004

The ASEAN countries developed their own guideline with more stressful stability testing than ICH and WHO recommended at that time. The reason for this decision was that the ASEAN regulators saw the need to address stability test conditions that reflect the natural meteorological conditions prevailing in the region. ASEAN humidity conditions are higher than in some regions that were previously defined as climatic zone IV.

The ASEAN guideline describes specifications for stability studies that have to be fulfilled in order to show that a product is stable over the entire period of its shelf-life. The guideline includes examples of a protocol of stability study, a report format, reduced design and extrapolation of data examples of packaging material parameters. These parameters include packaging material, thickness of packaging and permeability coefficient

Latest conditions measured by ASEAN nations showed that the average mean kinetic temperature is 27.76 °C and the average relative humidity (RH) is up to 78.79 (RH)%. Therefore the ASEAN stability guideline requires real time storage conditions for solid dosage forms with permeable primary packaging at 30°C ±2°C/75%RH±5% RH

At time of submission, it is required to provide 12 months real time data and a commitment to provide follow-up stability data for the rest of the shelf-life. Further at least 6 months accelerated stability data at 40°C ±2°C/75%RH±5% RH have to be provided with the marketing authorisation application. The selection of batches used for stability studies are 3 primary batches for NCEs and can be 2 pilot scale batches for generics and variations in conventional dosage forms. For products with impermeable primary packaging the storage conditions are 30°C ±2°C and can be any relative humidity.

The provision of stability data according to the ASEAN guideline will be mandatory with the implementation of the ACTD and ACTRs from January 2009. Currently discussions are on-going regarding the transition period. Until end of 2008 various storage conditions are accepted for filing. However companies are expected to have on-going stability data at 30°C/75RH beyond January 2009. Any filing after January 2009 must have stability data based on 30/75 conditions. Where products deteriorate at 30°C/75% RH it should be justified to label 'store below 25°C' or it should be ensured that moisture impermeable primary packaging is used [2]

INDIVIDUAL COUNTRIES REQUIREMENTS

MALAYSIA

Dossier Format:ACTD
Administrative Requirements

- ✓ Manufacturing license to be notarized.
- ✓ Certificate of Pharmaceutical Product issued by the competent authority in the country of origin according to the current WHO format – Notarized.
- ✓ Site master file of manufacturer not required.

Sample Requirement:No samples required for registration.
Product Registration Validity:5 years
Registration Lead Time: 180 Working days
Registration Fee:

- For single drug 2200 Malaysian Ringgit
- For 2 drugs 4000 Malaysian Ringgit

Submission Details: CD + Hard copy (Not complete dossier)

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Table 5: Part – I Of Actd Requirements For Malaysia

PART - I ADMINISTRATIVE DATA
Section A – Product Particulars
A1 Active Ingredients
A2 Excipients
A3 Dosage Form
A4 Product Description
A5 Pharmacodynamics
A6 Pharmacokinetics
A7 Indication
A8 Recommended Dose
A9 Route of Administration
A10 Contraindications
A11 Warnings & Precautions
A12 Interaction with other Medicaments
A13 Pregnancy and Lactation
A14 Side Effects
A15 Symptoms and Treatment of Overdose
A16 Effects on Ability to drive and use machine
A17 Preclinical safety data
A18 Instructions for use
A19 Storage condition
A20 Shelf life
A21 Therapeutic code
Section B – Product Formula
B1.1 Batch size
B1.2 Batch formula
B2 Batch Manufacturing formula and attachment
Section C – Particulars of Packing
C1 Pack size
C2 Immediate container type
C3 Container type description
C4 Barcode/ serial No. (if applicable)
C5 Recommended Distributor's Price
C6 Recommended Retail Price
Section D – Labels (Mock up)
D1 Label mock up for immediate container
D2 Label mock up for outer carton
D3 Proposed package insert
D4 Patient Information Leaflet
D5 Label mock up for Diluent
Section – E Supplementary Documentation
E 1.1 Product Owner
E 1.2 Letter of authorization from product owner
E 2.1 Letter of Appointment of Contract Manufacturer from Product owner
E 2.2 Letter of Acceptance from the Contract Manufacturer
E 3.1 Certificate of Pharmaceutical Product (CPP)
E 4.1 Certificate of Free Sales (CFS)
E 5.1 Certificate of Good Manufacturing Practice (GMP)
E6 Manufacturer
E7 Other Manufacturer (s) involved , if applicable
E8 Importer
E9 Store address

E10 Summary of Product Characteristics
E11 Company core data sheet
E12 Analysis protocol
E13 Protocol analysis and Data validation
E14 Other supporting documents
E15 Worldwide registration status
E16 Post approval commitment
E17 TSE- Risk Free Commitment

SINGAPORE

Dossier Format:ACTD
Administrative Requirements

- Manufacturing License not required.
- Certificate of Pharmaceutical product issued by the competent authority in the country of origin according to current WHO format- Notarized.
- Site Master File of Manufacturer is not required.

Sample Requirement: No samplesrequired for the Registration.
Product Registration Validity: 5 Years.
Registration Lead Time:240 Working days.
Registration Fee:

- For single drug 4400 Singapore dollars.

Submission Details:CD + Hard copy

Table 6: Part – I Of Actd Requirements For Singapore

PART I – ADMINISTRATIVE DOCUMENTATION
Section **1.0** Prism Application Form
1.0.1 Company Particulars
1.0.2 Applicant Particulars
1.0.3 Application Details
3.1 Type of Application
3.2 Type of Product
3.3 Reference Product
3.4 Product intended for Export
3.5 Type of Dossier
3.6 Type of Format
1.0.4 Product Information
4.1 Product Name
4.2 Product Formula
4.3 Ingredients derived from Human blood or Animal sources
4.4 Pharmacotherapeutic Group (ATC code)
4.5 Dosage Form
4.6 Route of Administration
4.7 Packaging, Shelf life & Storage Condition
4.8 Forensic Classification
4.9 Registration status in other countries
4.10 Product owner Information
1.0.5 Manufacturer's particulars
1.0.6 Information on company responsible for Batch release
1.0.7 Supporting Attachments

Section **1.1** Cover Letter
Section **1.2** Comprehensive Table of Contents
Section **1.3** Introduction
Section **1.4** Labeling and PIL proposed in Singapore
1.4.1 Outer Carton labels
1.4.2 Inner blister labels
1.4.3 Package Insert
1.4.4 Patient Information Leaflet (PIL)
Section **1.5** Approved SmPC
1.5.1 SmPC approved by HSA's reference regulatory agencies
1.5.2 SmPC approved by Country of Origin
1.5.3 SmPC approved by other Regulatory agency
1.5.4 Declaration that translation of SmPC currently conforms to the SmPC currently approved
Section **1.6** Assessment report issued by HSA's reference regulatory agencies
Section **1.7** Description of Batch Numbering system
Section **1.8** Proof of Approval from Country of Origin
Section **1.9** Proof of Approval from HSA's reference regulatory authorities
Section **1.10** Authorization Letters from product owner to the Applicant company
Section **1.11** GMP certification for each finished product manufacturer inclusive of secondary packers
Section **1.12** Patent Declaration Form
Section **1.13** Declaration on Rejection/with drawl and deferral
Section **1.14** Declaration that all aspects of Singapore product quality are identical to that of currently approved by the chosen primary reference regulatory agency
Section **1.15** Registration status in other countries as separate attachment in PRISM under "Supporting attachments"

THAILAND

Dossier Format:ACTD
Administrative Requirements

- Manufacturing License not required.
- Certificate of Pharmaceutical Product issued by competent authority in the country of origin according to current WHO format- to be Notarized.
- Site Master File of Manufacturer not required.

Sample Requirement:6 packs of samples required for registration.

Product Registration Validity:Life time (need to commercialize at least once in every 2 years to retain registration)

Registration Lead Time:110 Working days.
Registration Fee:For Single Drug 2000 Thai bhat.
Submission Details:CD + Hard copy

Table 7: Part – I Of Actd Requirements For Thailand

PART – I ADMINISTRATIVE DATA AND PRODUCT INFORMATION	
Section A Table of Contents	
Section B Guidance on the Administrative data and Artworks	
1	Certificate of Pharmaceutical Product
2	Artworks
2.1	Carton
2.2	Label
2.3	Package Insert

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PHILIPPINES

Dossier Format:ACTD
Administrative Documents:

- Manufacturing License should be Notarized.
- Good Manufacturing Certificate must be Notarized
- Certificate of Pharmaceutical Product must be provided in current WHO format

Sample Requirement:6 packs

Registration Lead Time:210 working days
Registration Validity: 5 years
Registration Fee:1052 US$
Strength wise separate dossier required
Number of copies to be submitted to MOH is one along with CD Format
Minimum stability data at the time of submission – 12 Months

Table 8: Part – I Of Actd Requirements For Philippines

PART – I ADMINISTRATIVE DATA AND PRODUCT INFORMATION
Section A Introduction
Section B Table of Contents
Section C Guidance on the Administrative data and Product Information
1 Application Form
2 Letter of Authorization
3 Certificates
a. Manufacturing License
b. Certificate of Pharmaceutical Product and GMP
c. Site Master File of Manufacturer
4 Labeling
4.1 Printed Carton
4.2 Printed Label
5 Product Information
5.1 Package Insert
5.2 Summary of Product Characteristics
5.3 Patients Information Leaflet

VIETNAM

Dossier Format:ACTD
Administrative Requirements:

- ✓ Manufacturing License should be Notarized.
- ✓ Certificate of Pharmaceutical Product issued by the competent authority in the country of origin according to current WHO format – Country specific and to be legalized from Vietnam embassy. (Qualitative and Quantitative composition should be attached duly attested by DCGI & Legalized.

Samples Required: Not required to be sent.
Registration Lead time:12- 18 months (without BE) 18- 24 months (with BE)
Registration Validity:5 years
Registration Fees:4,500,000 VND

Table 9: Part – I Of Actd Requirements For Vietnam

Section	Content	Remarks
PART – I	**ADMINISTRATIVE DATA AND PRODUCT**	
SectionA	Introduction	This section contains theAdministrativeDataandProductInformationwhic
SectionB	TableofContent	AsperACTD
SectionC	Guidanceontheadministrativedataand	
1	ApplicationForm(HandSigned	
2	LetterofAuthorization	
3	Certifications a) Mfg.License b) COPP(CountrySpecific) c) FSC(ifCOPP notavailable) d) Drug Trading Eligibility Certificates	Forimportedproducts: **a.** Notary only. **b.** Certificate of Pharmaceutical Product issued by the competent authority in the country of origin according to the current WHO format– Country Specific & to be legalized from Vietnam embassy.(Qualitative and Quantitative composition should be attached duly attested by DCGI & legalized) (or) FSC,GMPtobelegalizedfromVietnamembassy **c.** To be legalized from Vietnam embassy. **d.** Will be provided at country end.
4.	Labelling	3setsofexpectedlabel+1
5	Product Information 5.1 Package Insert 5.2 SummaryofProductCharacteristics (Product Datasheet) 5.3.PatientInformationLeaflet(PIL)	Package Insert is required for GenericproductsinEnglishwithseal(Translationwillbedoneatcountryend). NotapplicableforGenericdrugs. NotapplicableforGenericdrugs.

SUMMARY

Malaysia

- From the above comparison table, it is clearly evident that, drug registration requirements for Malaysia are more or less the same to other member countries, the only major difference is in the Part – I of ACTD, also to submit the Table of contents section, which is unique for Malaysia.

Singapore

- One unique requirement for Singapore, it accepts either ACTD/CTD

- In ACTD, we are supposed to submit COVERING LETTER in PART – I, which is the major difference for Singapore and other member countries.
- Samples are not required during filing.

Thailand

- The product registration validity which is lifetime for Thailand whereas we need to commercialize the product at least once in every 2 years to retain registration.
- 6 packs of samples are submitted during filing

Philippines

- To conduct Audit at the Finished product plant, the plant should to be registered at the Philippines Ministry of Health, which is unique for Philippines
- 6 packs of samples should be submitted at the time of filing for drug registration.

Vietnam

- One unique requirement for Vietnam is the COPP (Certificate of Pharmaceutical Product) should be legalized. The other requirements of Vietnam are more or less the same when compared to its member states.

Table 10: Comparison Of Part – I Requirements Between Malaysia, Singapore, Thailand, Philippines, Vietnam [4]

Country	Malaysia	Singapore	Thailand	Philippines	Vietnam
Cover letter	×	√	×	×	×
Table of contents	×	√	√	√	√
Application Form	×	√	×	√	√
Product Information	√	√	×	√	√
GMP Certificate	√	√	×	√	×
Certificate of Suitability (CEP) if any	×	×	×	×	×
COPP	√	√	√	√	√ - Legalized
Patent Declaration Form	×	√	×	×	×
Free Sale Certificate	√	×	×	×	√
Site Master File	×	√	×	√	×
Labelling	√	√	√	√	√
Registration Status in other Countries	√	√	×	×	×
Manufacturing License	×	×	×	√	×

CONCLUSION

The individual country requirements for drug products registration were compared; the differences in their requirements for drug products registration was demarcated. The important differences include

- Countries differ in drug product registration time and approval
- Individual and separate filings for each country, which results in cumbersome process for the applicant to file separately for each individual country.
- Some countries differ in the format of dossiers submitted, where as some follow electronic submissions and other countries require paper submission, which results in the delay of preparation of dossier and delay in the filing of submissions and delay in the approval.

- There is no single window clearance system, where as each country should individually review the dossier, processed and get multiple clearances from different departments of the regulatory body of that country.

To overcome the above mentioned differences between the countries for fast approval a Unified Harmonization Plan is proposed

- ✓ All the countries should be able to accept electronic submissions of dossiers which results in fast filing and further results in fast review and fast approval of drug products filed for registration, which results into the condition where the people of ASEAN nations have early access to safe, efficacious and quality medicines.
- ✓ Establishment of single window clearance system will save the resources and time of the ASEAN nations during the time of review and approval of dossiers.
- ✓ If the Approval system is Fast and stringent, more companies would like to foray into the market of ASEAN nations where people of ASEAN nations will have access to medicines even for diseases which are considered least important (orphan drugs in case of US)

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