SITUATION ANALYSIS OF DRUG PRODUCT INFORMATION PROVISION IN YANGON AND REVIEW ON CONSUMER DRUG INFORMATION GUIDELINES ACROSS COUNTRIES

Miss Zar Ni Win

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Social and Administrative Pharmacy
Department of Social and Administrative Pharmacy
FACULTY OF PHARMACEUTICAL SCIENCES
Chulalongkorn University
Academic Year 2019

การวิเคราะห์สถานการณ์การให้ข้อมูลผลิตภัณฑ์ยาในย่างกุ้ง และการทบทวนแนวทางการทำเอกสารข้อมูลยาสำหรับประชาชนในประเทศต่าง ๆ

น.ส.ซิน นิ วิน

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาเภสัชศาสตร์สังคมและบริหาร ภาควิชาเภสัชศาสตร์สังคมและบริหาร
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2562

Thesis Title	SITUATION ANALYSIS OF DRUG PRODUCT INFORMATION PROVISION IN YANGON AND REVIEW ON CONSUMER DRUG INFORMATION GUIDELINES ACROSS COUNTRIES
By	Miss Zar Ni Win
Field of Study	Social and Administrative Pharmacy
Thesis Advisor	Associate Professor Police Lieutenant PUREE ANANTACHOTI, Ph.D.

Accepted by the FACULTY OF PHARMACEUTICAL SCIENCES, Chulalongkorn University in Partial Fulfillment of the Requirement for the Master of Science

..... Dean of the FACULTY OF PHARMACEUTICAL SCIENCES
(Assistant Professor RUNGPETCH SAKULBUMRUNGSIL, Ph.D.)

THESIS COMMITTEE

..... Chairman
(Assistant Professor RUNGPETCH SAKULBUMRUNGSIL, Ph.D.)

..... Thesis Advisor
(Associate Professor Police Lieutenant PUREE ANANTACHOTI, Ph.D.)

..... Examiner
(Associate Professor Police Captain TANATTHA KITTISOPEE, Ph.D.)

..... External Examiner
(Mohd Shahezwan Abd wahab, Ph.D.)

ซิน นิ วิน : การวิเคราะห์สถานการณ์การให้ข้อมูลผลิตภัณฑ์ยาในย่างกุ้ง และการทบทวนแนวทางการทำเอกสารข้อมูลยาสำหรับประชาชนในประเทศต่าง ๆ. (SITUATION ANALYSIS OF DRUG PRODUCT INFORMATION PROVISION IN YANGON AND REVIEW ON CONSUMER DRUG INFORMATION GUIDELINES ACROSS COUNTRIES) อ.ที่ปรึกษาหลัก : รศ. ภญ. ร.ต.ท.หญิง ดร.ภูรี อนันตโชติ

ข้อมูลที่ไม่ครบถ้วนและไม่เพียงพอเกี่ยวกับการใช้ยานำไปสู่ผลลัพธ์ที่ร้ายแรงต่อสุขภาพและผลทางเศรษฐกิจการศึกษาก่อนหน้าแสดงให้เห็นว่าผู้บริโภคจำนวนมากทานยาโดยไม่ทราบว่ายาถูกต้องหรือเพียงพอในขณะที่ผู้บริโภครายอื่นไม่มีความรู้เกี่ยวกับความเสี่ยงของยาในความเป็นจริงผู้บริโภคทุกคนมีสิทธิที่จะรู้เกี่ยวกับข้อมูลของผลิตภัณฑ์ที่พวกเขาได้รับและการใช้ยาที่เหมาะสมและการรักษาที่ประสบความสำเร็จขึ้นอยู่กับวิธีที่ผู้ป่วยจัดการยาด้วยตัวเองเมื่อผู้ป่วยต้องพึ่งพาตนเองความรู้ด้านการดูแลสุขภาพและข้อมูลยากลายเป็นสิ่งสำคัญสำหรับพวกเขาการวิเคราะห์เนื้อหาและการสำรวจผู้ป่วยจำลองเพื่อประเมินสถานการณ์ปัจจุบันเกี่ยวกับการจัดหาข้อมูลผลิตภัณฑ์ยาสำหรับผู้บริโภคชาวพม่าโดยใช้ตัวอย่างยา30รายการในสามกลุ่มยาเพื่อประเมินข้อมูลผลิตภัณฑ์ยาการสำรวจผู้ป่วยจำลองมาตรฐานได้ทำการประเมินข้อมูลยาและคำพูดด้วยการใช้ Mefenamic Acidที่ให้ไว้ในร้านขายยาชุมชนรอบๆย่างกุ้งในขั้นตอนที่สองของการศึกษาครั้งนี้มีการทบทวนวรรณกรรมเป้าหมายเพื่อระบุและเปรียบเทียบกฎระเบียบที่แตกต่างกันของแนวทางการพัฒนาPILและPILในแง่ของเนื้อหาการออกแบบและการทดสอบผู้ใช้ในประเทศต่างๆการวิเคราะห์เนื้อหาของผลิตภัณฑ์ยาพร็อกซี30รายการพบว่ามากกว่า80%ให้ข้อมูลเป็นภาษาอังกฤษทั้งในกล่องกระดาษและในแผ่นพับแผ่นพับส่วนใหญ่(87%)มีไว้สำหรับผู้เชี่ยวชาญด้านการดูแลสุขภาพไม่ใช่สำหรับผู้บริโภคผลจากการศึกษาผู้ป่วยจำลองพบว่าผู้จำหน่ายยาส่วนใหญ่ไม่ได้ถามผู้ป่วยแต่ประวัติความเหมาะสมของยาเสพติดในขณะที่กว่า95%ให้ข้อมูลด้วยวาจามีความแตกต่างอย่างมีนัยสำคัญทางสถิติในคะแนนเฉลี่ยของข้อมูลยาเสพติดเป็นลายลักษณ์อักษรโดยเภสัชกรและไม่ใช่เภสัชกรสรุปได้ว่าผู้บริโภคชาวพม่าไม่ได้รับข้อมูลยาเพียงพอจากผลิตภัณฑ์และผู้จำหน่ายดังนั้นจึงควรมีการใช้PILเพื่อความปลอดภัยในการใช้ยาของผู้ป่วยการทบทวนวรรณกรรมเป้าหมายส่งผลให้มีแนวทาง12PILและมีเนื้อหาและการออกแบบที่คล้ายกันระหว่างประเทศแต่มีเพียง5แนวทางที่กล่าวถึงการทดสอบผู้ใช้PILโดยรวมแล้วมีข้อเสนอแนะว่าแนวทางของสหราชอาณาจักรเป็นแนวทางที่เหมาะสมและเชื่อถือได้เพื่อใช้เป็นข้อมูลอ้างอิงสำหรับประเทศอื่นๆในการพัฒนา PIL ของตนเอง

สาขาวิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่อนิสิต .....

ปีการศึกษา 2562 ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

6176354533 : MAJOR SOCIAL AND ADMINISTRATIVE PHARMACY
KEYWORD: DRUG INFORMATION/ MYANMAR CONSUMERS/ SIMULATED PATIENT METHOD/ PATIENT INFORMATION LEAFLET GUIDELINE

Zar Ni Win : SITUATION ANALYSIS OF DRUG PRODUCT INFORMATION PROVISION IN YANGON AND REVIEW ON CONSUMER DRUG INFORMATION GUIDELINES ACROSS COUNTRIES. Advisor: Assoc. Prof. Pol.Lt. PUREE ANANTACHOTI, Ph.D.

The appropriate drug use and successful treatment relies heavily on how patients administer medicines by themselves and thus healthcare knowledge and drug information become crucial for them. Firstly, content analysis was conducted to evaluate drug product information attached with the 30 drug samples of three drug classes. To evaluate written and verbal drug information, standardized simulated patient survey was conducted by using Mefenamic Acid provided in community pharmacies around Yangon. In the second step of this study, targeted literature review was performed to identify and compare different regulations of PILs and PIL development guidelines in terms of contents, designs and user testing across various countries. The content analysis of 30 proxy drug products showed that more than 80% provided information in English, both on carton boxes and in leaflets. The majority of the leaflets (87%) were only intended for healthcare professionals. The survey in Yangon found that most dispensers did not ask patients about their history for the appropriateness of the drugs whereas more than 95% of them provided verbal drug information. There was a statistically significant difference in mean scores of written drug information provided by pharmacists and non-pharmacists. It was concluded that Myanmar consumers did not get enough drug information from the products and dispensers and thus there should be implementation of PILs for patient's safe use of drugs. The targeted literature review resulted in 12 PILs guidelines and there had been similar contents and designs among countries. But there were only 5 guidelines that mentioned about user testing of PILs. Overall, it was suggested that UK guideline was a suitable and reliable guideline to use as a reference to develop PILs.

Field of Study:	Social and Administrative Pharmacy	Student's Signature .....
Academic Year:	2019	Advisor's Signature .....

ACKNOWLEDGEMENTS

This thesis could not appear without the support and guidance from a number of people. I would like to express my sincere thanks and deep gratitude to the following people who made this academic work possible.

First of all, I would like to express my deepest appreciation to my advisor, Assoc. Professor Puree Anantachoti, Ph.D., who supported me throughout my thesis with her remarkable patience. Without her unwavering guidance, encouragement and great efforts, my research would not have been completed. I would also like to extend my thanks to Asst. Prof. Rungpetch Sakulbumrungsil, Ph.D., Assoc. Prof. Tanattha Kittisopee, Ph.D., and Dr. Mohd Shahezwan Abd Wahab, Ph.D., my thesis committee members, for their constructive comments and valuable suggestions.

Secondly, I would like to give special thankfulness to the Chulalongkorn University for giving me an opportunity to join the ASEAN scholarship program and for the financial support to study this Master Degree.

In addition, I am also grateful to all the authorities from Department of Food and Drug Administration, Myanmar for their invaluable advice and guidance in the process of trying to get Ethical Approval from the Ministry of Health and Sports, Myanmar.

I do not leave my special appreciation to all the faculty members and staffs from the Graduate Program of Social and Administrative Pharmacy, Faculty of Pharmaceutical Sciences. I also want to thank my forever friend, Mocha, who never fails to support, encourage and upraise me throughout my challenging moments. Finally, I feel thankful to my family members and also classmates who ever help me whenever I need them.

Zar Ni Win

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Table 4.3 Common and Similar Contents in PILs of all 12 guidelines

LIST OF ABBREVIATIONS

ACTD	ASEAN Common Technical Document
ADR	Adverse Drug Reaction
ASEAN	Association of South East Asian Nations
CMI	Consumer Medicine Information
CTD	Common Technical Document
DRA	Drug Regulatory Authority
EC	European Commission
ECP	Emergency Contraception Pill
EMA	European Medicine Agency
EU	European Union
FDA	Food and Drug Administration
FGD	Focus Group Discussion
GDP	Gross Domestic Product
GERD	Gastroesophageal Reflux Disease
GPP	Good Pharmacy Practice
IFU	Instruction for Use
KAP	Knowledge, Attitude and Practice
MG	Medication Guide

MIMI	Master Index of Medical Specialties
MPMEEA	Myanmar Pharmaceutical and Medical Equipment Entrepreneurs Association
NSAID	Non-Steroidal Anti-Inflammatory Drug
OPD	Outpatient Department
OTC	Over the Counter
PI	Package Insert
PIL	Patient Information Leaflet
POM	Prescription only Medicine
PPI	Patient Package Insert
RDU	Rational Drug Use
RHC	Rural Health Centre
SmPC	Summary of Product Characteristics
TGA	Therapeutic Goods Administration
UK	United Kingdom
US	United States
USD	United States Dollar
WHO	World Health Organization
WMI	Written Medicine Information

CHAPTER I - INTRODUCTION

1.1. Background and rationale

In most of the developing countries, irrational drug use problems have occurred due to health care professional shortage, inadequate public financing support, poor knowledge and literacy problems of patients (1). Since patients are the last responsible bodies in medication use cycle, the greatest outcomes of the medication treatment could not be achieved if they do not know how to use their drugs (2). But, they only remember about 20% of medicine information which they receive from their physicians during consultation time (3). Moreover, previous studies showed that many consumers took without knowing their medicines correctly or sufficiently while other consumers did not have knowledge about the risks of their medicines (4-6). In fact, all consumers have the right to know about the information of the products they receive and appropriate drug use and successful treatment relies heavily on how patients administer medicines by themselves (7). When patients have to rely on themselves, healthcare knowledge and drug information become crucial for them.

Generally, there are two main types of drug information. The first one is intended to be used by health care professionals and the other is for patients, consumers and care givers. The drug information for health care professionals has been called differently, such as Summary of Product Characteristics (SmPC) in the European Union (EU) or Package Insert (PI) in Australia. SmPC has been mentioned in

the administrative part of the Common Technical Document (CTD) and has been required by many Drug Regulatory Agencies (DRAs) as a part of registration dossier to get market approval (8). The objectives of SmPC are to provide the scientific information such as quantitative and qualitative composition, pharmaceutical properties, as well as clinical and pharmacological particulars for health care professionals (9). Because of this kind of complex drug information provided in SmPC, it is not efficiently beneficial and understandable for lay people.

The use of drug information for patients or lay people was initiated by the United States (US) in the early 1980's (10). Patient Information Leaflet (PIL) is an educational material that provides drug information for patients in lay language to ensure proper medicine use. It usually consists of drug information such as dosage regimen, precautions, potential side effects and interactions with other drugs or foods (11). The terms used for PIL differ among countries such as PIL" in the Association of Southeast Asian Nations (ASEAN), "Consumer Medicine Information, CMI" in Australia. They can be found as a paper in the drug products' carton box or can be assessed on the DRA websites of some countries like Australia and the UK (12-14). As the implementation, regulations and guidelines used for PILs development are also varied among countries, PILs designs, contents and user testing might not be the same.

In the development of PILs, designs and contents are important factors which can determine whether a PIL will be read or discarded by consumers. A study on the

evaluation of PILs showed that about 34.5 % of patients never like to read PILs because of difficulty in understanding leaflet contents and complained about the difficulty in reading due to the long papers with small print and poor quality (15). On the other hand, the evaluation of PIL also plays a necessary role to improve its usability and understandability, but the methods used can vary significantly. Legislation of PILs in some countries are concerned about the evaluation and it is a mandatory requirement that manufacturers have to test their PILs by using consumer user-testing before they get approved as in the EU (16). User testing is most commonly used and an effective method to investigate the performance of PILs regarding consumers' ability to find and understand medicine information from the leaflets (17-19).

Not only the high-income countries, such as the US and Australia, implemented regulations of PILs, other middle-income countries of ASEAN including Thailand and Malaysia started to use PILs. The members of ASEAN started to implement the use of ASEAN CTD (ACTD) format for marketing authorization approval in December 2008. PIL was also mentioned in ACTD, but without describing detailed information about how to develop and test the PILs. Additionally, the regulations and guidelines used for the pharmaceutical products including legislations of PILs are different among member countries (20).

Myanmar, a member of ASEAN, has over 53 million populations with GDP of 1,161.5 USD per capita. Healthcare expenditure accounted for only 2.3% of the GDP

which is considered lower than the WHO recommendation. The government spends only 3-5% of health care budget on medical goods and a larger share is given to other health related activities including education and training of health personnel and environmental health (21). The provisions of healthcare medical supplies to the citizens are not top priority and thus patients usually have to pay out of pockets to get their prescriptions which are filled at drugstores.

Many drugstores in Myanmar do not have pharmacists on duty because of shortage in pharmacist workforce. A study on perception and practice of drug sellers on antibiotic sales without prescription in Yangon region showed that only 4.9% of drug sellers were trained pharmacists who could give the right information about the role of antibiotic resistances (22). Another similar study which was conducted in Nyaung Lay Pin Township also found that there were no proper pharmacists and only about 43.3 % of dispensers got about 3 months-training from the private pharmacy training school. Consequently, the process of dispensing and provision of drug information are mostly done by compounders of 3 moths to 1-year training and other non-health care professional staffs in the community pharmacies and outpatient department (OPD) pharmacies of public hospitals (23).

Since 1993, Myanmar FDA established the order no 7/93 of Regulations on Myanmar National Drug Law which mentioned that all the labels on outer package and package inserts must be described in Myanmar or English or both languages (24). In addition, labeling requirements for consumer products of Consumer Protection

Law, 2019 state that all the labels of over the counter medicines and food supplements must be described in Myanmar language (25). According to this law, some pharmaceutical companies are trying to provide Myanmar language labels by directly translating from English PI when they seek for marketing authorization approval. However, all importers of the pharmaceutical companies cannot provide PI and SmPC in Myanmar language and that of other prescription medicines are still in English language. In real practice, patients normally do not get that kind of information since they usually buy only a small number of medicines, not the whole carton box.

Myanmar has continuously experienced healthcare professional shortage, inadequate healthcare budget and inadequate supply of medicines, so patients and consumers in the country have to buy medicines from the private pharmacies and rely heavily on drug information provided to them. Thus, it is important to evaluate the current situation of drug information handling in community pharmacies of Myanmar. In addition, guideline, regulation and practical enforcement for PILs has not been developed yet although it was described in guideline on drug registration application of Myanmar FDA. The detailed description of contents and designs for PILs have not found in any laws or regulations of Myanmar. If drug information for patients is needed, it will become crucial to determine which contents and designs are suitable for Myanmar people.

Moreover, there were a number of researches which focused on development, user testing and consumer perspectives of PILs in many countries and many reviews for the establishment of best practices of PILs design (26-28). But, the results from those studies did not include how PILs are regulated and how they are developed among various countries. Other DRAs or researchers who intend to create PILs or guidelines by their own might not able to easily assess and grasp those kinds of information from those studies. Therefore, the review on international regulations and guidelines of PILs would be a first step to understand how other countries regulate, develop and test PILs which could lead to create Myanmar's own PILs guideline.

1.2. Research questions

- Are the consumers in Myanmar getting enough information from the drug products and community pharmacies for their medication usage?
- What are the differences in regulations and guidelines of PILs across various countries?

1.3. Objectives

- To assess current situation regarding provision of drug product information for Myanmar consumers.

- To identify and compare different regulations of PILs and PIL development guidelines in terms of contents, designs and user testing across various countries.

1.4. Expected benefits and applications

The results from this study stated that drug information provided with the drug products were not usable and appropriate for the use of lay people in Myanmar. Moreover, Myanmar consumers did not get enough information about the drugs from dispensers in community pharmacies. It also provided that there were not sufficient pharmacists on duty in the community pharmacies. Therefore, it could highlight the need to have stricter regulations at community pharmacies in Myanmar, so that pharmacists will be available on-site and educate or motivate both pharmacist and non-pharmacist dispensers to provide drug information to consumers. Additionally, different regulations and guidelines of PILs across various countries and the strength and weakness of PIL development guidelines could be known which in turn would provide knowledgeable information to create our own PIL development guideline.

CHAPTER II- LITERATURE REVIEW

The objectives of this study were to assess current situation regarding provision of drug information to Myanmar people at community pharmacies in Yangon region and to review and identify different regulations of PILs and PIL development guidelines in terms of contents and designs across various countries. This chapter encompassed a review of the related literatures to facilitate the assessment of problems with insufficient medicine information, types of different drug information and the identification of regulations and guideline developments of PILs. The reviews of literatures covered the following issues:

1. Medication use problems in patients
2. Types of drug information in various countries
3. Importance of medicine information in medication use cycle
4. Relevant researches
5. Current situation of pharmaceutical regulations and drug product information in Myanmar

2.1. Medication use problems in patients

More than 50% of medicines are prescribed, dispensed or sold inappropriately and 50% of patients fail to take them correctly. The main causes of these problems include healthcare professional shortage, inadequate public financing support, poor knowledge and literacy problems of general population. Adverse

events and medication errors resulting from inappropriate administration of medicines are a serious concern since patients play major roles in medication use and they need to manage multiple prescription and OTC medicines. So, patients understanding about medication use is essential for their adherence and the developed countries like the UK and USA, they set up patient safety as first priority in healthcare system (29).

The therapeutic effect of medicines can be observed by the correct and efficient usage and many steps involved in medication use. The very common and important steps included are reading and understanding instructions for use, handling outer packaging, handling immediate packaging, preparation prior to use and drug taking by the patients. Previous studies showed that patients experience medication use problems, such as difficulties in accessing the contents and identification of medicines, difficulties in swallowing of medicines and most common in elderly patients (30, 31).

Problems with inappropriate medication use are very common, especially in developing countries and this can lead to reduction in the quality of pharmaceutical therapy, increase in cost of health care, increase in risk of undesired effects such as adverse drug reactions (ADRs) and antimicrobial resistance (32). Generally, the process of medication treatment includes prescribing, documenting, dispensing, administering and monitoring and errors in medicine use or medication problems can occur at any of these stages. A study on incidence and preventability of ADRs and

potential ADRs concluded that prescribing might account for 49% of significant errors comprising, administration, dispensing and documenting for 26%, 14% and 11%, respectively (33).

The main stakeholders in the cycle of medication usage are healthcare professionals and patients are the last people in this cycle. Thus, healthcare professionals as well as patients are also responsible for minimizing the number of medication errors (34). The medication use problems which occur in patients could relate to insufficient medicine information, inadequate time to contact with healthcare professionals to provide information, and low healthcare literacy of patients. The process of medication use by patients may be complex and include various activities in which medication errors occur. The adverse drug effects caused by patient errors might be reduced by developing and maintaining safe medication-management systems and providing sufficient information about the medications (35).

The effective communication between patients and healthcare professionals is one of the major elements to improve the healthcare quality. The limited consultation time and the working style of physicians could influence the communication and the physicians commonly do not provide information about the precautions to be taken or undesired effects in the course of the treatment (36). The medication mistakes of patients were associated with not considering the prescriptions of other physicians, inconsistency in the information or being treated by

various physicians at the same time and continuous changes in prescription. The patients would take the wrong medicines or make mistakes about the medication uses if the physicians do not clearly explain how to take medicine or do not give clear instructions about the medication use (37). All of these problems are linked to the failure in communication between healthcare professionals and patients.

The problems of medication usage by patients might also be influenced by their poor knowledge and low health literacy. The health literate patients could use their skills for self-efficacy and empowerment in health- related decisions. Most patients have suggested providing a repeated message by personalized counselling on medications especially on initial therapy by improving verbal and written information for their understanding of medication usage. It was also recommended that written information and instructions are valuable sources of medication information supplementary to verbally communicated instructions, if general practitioners and pharmacists do not provide sufficient instructions for medicine consumers (38).

2.2. Types of drug information in various countries

Normally, there are two main types of drug products information other than the labelling information on the outer carton box. As described in the administrative information and prescribing information of CTD, the first one is generally called as SmPC or package insert (PI) which gives the technical information for medical

practitioners, pharmacists and other prescribers about the risks and benefits of the product and supports them to give pharmaceutical education for patients. The other type of drug product information is for patients and it provides information about the medication usage in lay language for the safe and effective use of medicines. However, the module 1 of CTD is region specific and thus the requirements and types of product information might be different depending on regulations of countries which give market approval (8).

2.2.1. Canada

According to Health Canada, information for drug products is called product monograph and is defined as a fact-based, scientific document that, does not mention any advertising content, contains the properties, claims, indications, and usage of the drug, and consists of other information necessary to use the drug optimally, safely and effectively. Each product monograph contains three distinct parts: health professional information in Part I, scientific information in Part II and information for consumer in Part III. Part I of product monograph contains information which is required for healthcare professionals to prescribe and dispense the medication safely and appropriately. The scientific information in Part II is the extended information of Part I. It describes more comprehensive and thorough research information including toxicology and data from studies in animal and clinical trials in humans. Part III, information for consumers, contains information

obtained from Part I and II which helps the consumers to understand what the medication is, how to use it and what kinds of side effects are possible. It is also considered to guide health professionals to easily identify the information which is required for counselling patients (39).

2.2.2. The European Union (EU)

Drug information for human medicines in EMA included three types: labeling, SmPC and package leaflet. Labeling is the information provided on the immediate or outer package of a medicine and SmPC provides basic information for healthcare professionals and basis for the preparation of package leaflet. Package leaflets are important documents to provide information on medicines for end-users (9). From these examples, drug information available includes health professional information and consumer medicine information. Mostly, outer labels and SmPC are provided with the drug products in all countries, but inclusion of leaflets for patients varies. In almost all the members of EU, and the EMA the drug package leaflets are usually provided not only with the drug products but also can be found on the websites of their regulatory agencies (40).

2.2.3. The United States (US)

In US FDA, it was described that all drug products imported into the US (United States) are subjects to labeling requirements and drug labeling requirements which depend on the type of drug product (41). For patient labeling in US FDA, it consists of three sub-types: medication guides (MG), patient package inserts and instruction for use (IFU). Medication guides are primarily for prescription products with serious and public health concerns and based on professional information. Patient package insert is part of prescription drug labelling approved by FDA. They are developed by the manufacturer and are required to be dispensed with the specific or classes of products. Instructions for use are also developed by the manufacturer, approved by the FDA, and dispensed with specific products with complex instructions for dosage to help appropriate patient use of the product (42).

2.2.4. Australia

The medicine information and labeling of Therapeutic Goods Administration in Australia are part of CTD module 1 and comprise of three main parts. These are product information and package insert, consumer medicine information and label mock-ups and specimens. Product information and package inserts are objective information that contains the quality, safety and efficacy of the product and intended to support as a guide for doctors, pharmacists and other health professionals in the process of prescription and dispensing of medicines. Consumer

Medicine Information is leaflet that provides information on the safe and effective use of a prescription or specified over-the-counter medicine for the consumers. Medicine labels appear on the outer carton of each medicine and help to find medicines easily (43).

2.2.5. The ASEAN

While observing the product information in ACTD guidelines which are used in ASEAN countries, it includes package insert, SmPC and PIL. In the package insert, the information provided is intended for healthcare professionals and PILs are the version for patients adapted from package inserts. SmPC is the product data sheet and includes the scientific information such as quality and quantitative composition, pharmaceutical form, clinical particulars and pharmacological properties (14). The administrative part of product information describes that language used can be English and/or official native language for all types of product information. But it is mentioned NCE and biotechnology products while PIL is only required for OTC products (44). However, the regulations used for product information especially PILs are not the same among ASEAN countries.

As an example, the Singapore Health Science Authority (HSA) defines labelling as any printed or graphic information on the immediate container, outer packaging and any other form of printed material supplied together with the product. The product labels of pharmaceutical products include outer carton and inner/ blister labels, PI and PILs are included. The outer carton is defined as the packaging of

product in which immediate packaging is placed, e.g. the carton box which consists of blister strips. If the label is affixed to the primary container of the product, this is called ‘inner label’, e.g. the label that fixed to a vial, ampoule or bottle. And the foil packaging of a blister strip is regarded as ‘blister strip’. The PI refers to a paper document consisting of scientific, objective account of the medicine’s usefulness to ensure the safe and effective use of a therapeutic product. The information provided in the PI shall not be promotional in nature. The PIL which is consistent with the product label and/or PI is intended for the patients and must be easily understandable (45).

On the other hand, patients receive different forms of information for their medication use. This include verbal information given by physicians during counselling, written and verbal information provided by dispenser, patient information leaflets included along with provided drugs, free information sources which are available online and information provided by the specific websites of DRAs.

2.3. Importance of medicine information in medication use cycle

Labeling and packaging deficits remain the common sources of system failure that lead to medication errors which are the significance of morbidity and mortality and estimated to cost billions of dollars a year in the United States alone. Confusion due to similar appearances for medication packages, or similar labels for different

medications have been contributed to 33% of medication errors and confusion due to medication names cause 12-25% of errors in the United States. Even though there has been an argument for having different medications packed in a similar fashion can increase risk of medication confusion, and many iatrogenic injuries have resulted from the poor system such as similar medication packages for different drugs, similar names for drugs with opposite effects (46).

Since physicians may not have sufficient time for consultation with patients, there may be difficulties in giving medical information to patients. Mostly in the emergency department, information given by physicians is essential and if patients did not get enough information, they could get many complications. To overcome this kind of problems, giving medicinal information by other ways such as providing PILs is suitable. A previous study in France showed that among the tested 324 participants, the mean doctor-patients communication scores was improved with the use of PILs. The good communication was about two times better in the group using PILs. PILs could also improve the timely use of medications and satisfaction with healthcare professionals. If doctors use PILs, the use of prescribed drugs also reduced, and patient's need for new medical consultation was decreased (47).

Community pharmacists may also face drug-dispensing problems from a patient's discharge from hospital. If patients are not given any information about their medication after hospital discharge, there may be a higher risk of difficulties related to prescription quality or various logistic concerns. The discontinuation of

their treatment and serious clinical implications may result from not timely showing up by many patients with their prescription at community pharmacies. For the improvement of patient care by community pharmacist, there should be sufficient information provided by healthcare professionals from hospitals (48).

A study conducted on cross-sectional survey of patient's needs for information and support with medicines after hospital discharge showed that many patients did not feel involved in prescribing decisions made during their hospital stay and a minority of patients discussed about their medicines with any health professional. However, there was variation between medicines information provided during hospital stay and after discharge. Pharmacists should have involved in the hospital and community settings and developed their roles to support patients with their medication information (49).

Patients are the last responsible bodies in the medication process life cycle and so about 3% of medication errors may be reduced by raising their awareness about their treatment, by being actively participating in ensuring continuity of care, and by informing them. Although conversation between patients and healthcare professionals during counselling is essential, health-care professionals often think that the quality of information they provide may be sufficient even patients would like to know more about their medicines. Therefore, clearly understandable information for patients about their medicines are needed and thus clearly stated

patient information leaflets (PILs) are necessary sources of information for patients and care givers (50).

Besides, a South-Indian based study involved testing the usefulness of PILs by administering the knowledge, attitude and practice (KAP) questionnaires to the patients with chronic diseases. That study evaluated patient's knowledge about the medications at pre and post administration of PILs. It was found that the provision of PILs could significantly increase KAP scores of patients, so they could correctly self-administer their medications (51). Another study proved that the use of appropriately designed leaflets has an advantage on medicine taking behavior and participants' medicine knowledge was significantly improved after receiving leaflets (52). PILs might be considered as a useful tool especially for patients with acute conditions where they first suffer from lack of medicine information. The improvement of patients' knowledge ranged from 18 to 57% with detailed description and graphical presentations of leaflets (53). A randomized controlled trial of pictogram-based intervention also concluded that the use of plain language, pictogram-based medication counseling could decrease medication dosing errors and improve adherence (54).

2.4. Relevant researches

Since this research study targeted literature review on patient information leaflets guidelines and shopping as a simulated patient, the literature review included simulated-patient method and researches related to both parts.

2.4.1. Simulated-patient method

The observational research techniques can be used to detect which medicines are being sold, prescribed or use and what type of information on the use of medicines are provided by the dispensers or sellers. However, the study may be difficult to carry out if the sellers or dispensers know and they may feel that this study will endanger their business. Besides, they may overact or cannot get the actual results if they know the presence of researchers. To overcome this kind of difficulties, simulated client method is most commonly used to study drug information provision study especially at the community pharmacies. By conducting this method, unbiased picture of normal drug information provision can be known (55).

In secret shopping process, a secret shopper (also known as mystery shopper, simulated patient or pseudo-patient) enters into a pharmacy shop and make a communication with a staff. In general, a secret shopper should not be identifiable as a regular patient (56). They are trained to visit a pharmacist to enact a scenario that assesses the specific behavior of pharmacy staff. The objective of simulated patient

method is to evaluate how the dispensers provide drug information for the patients and how they react to the patients' complaints (57).

The use of simulated patient visits has many advantages than other kinds of methods that use to investigate the practices of pharmacy staffs. By using this method, the natural context of drug use can be observed. The results from method can provide more reliable information than interviews and can also be generalized and quantified (55)Although simulated client method is a useful way to study the planning services and behavior of pharmacists or drug dispensers, there are some limitations such as difficulty in data interpretation and the short period of observations. Some of the findings are also needed to complement by adding another method including interviews(58).

2.4.2. Dispensing practices and simulated-patient studies in community pharmacies

The irrational drug use problem was considered as a major problem in worldwide and it was estimated that more than 50% of medicines were used irrationally. The problem of irrational drug uses was associated with use of too many medicines, health care professional shortage, inadequate public financing support, poor knowledge and literacy problems of general population. Therefore, many kinds of solutions are needed, including the good communication between physicians, pharmacists and patients as teamwork. To give correct drug and drug information to

the right patients, Good Pharmacy Practice also plays an important role to stimulated rational drug use (RDU) (59, 60). In this manner, the study of dispensing practices in community pharmacies become vital for the medication use cycle including patients who are the last responsible persons and pharmacist who are the last healthcare professionals in the medication use cycle (61).

There are many researches that evaluated the dispensing practices in community pharmacies. One study of performing on dispensing practices of antibiotics included 161 community pharmacies from two districts of Nepal. They investigated not only the dispensing practices of pharmacy staffs but also the status of pharmacies. It was described that almost two-thirds of pharmacies had licenses. They found that about 63.6% of pharmacy staffs had Community Medical Assistance Degree and there was a relationship between qualification of pharmacy staffs and location of pharmacy (rural vs. urban). Among all pharmacy staffs, only 8.6% were pharmacists. The practices of dispensing antibiotics without prescription were also significantly associated with working experiences and age of staffs (62).

Another study of pharmacists' opinion on dispensing antibiotics without prescription suggested that pharmacist on duty should be present in the community pharmacies to control drug consumption of patients. They also found out that pharmacist's workload was needed to optimize, and the collaboration of physicians and pharmacists was necessary (63).

In an Ethiopia study, a cross-sectional study was performed in 15 community pharmacies and included 255 clients. Out of a total of 18 dispensers, there were only 3 pharmacists and 5 dispensers were not professionally qualified. Ninety percent of clients answered that they were not asked for their identity such as age. This study concluded that most of the dispensing practices were substandard and suggested that to give some educational program or policy management for good dispensing practices in their country (64).

A number of researches had also been performed by secret shopping at pharmacies for many purposes including assessing dispensing skills and of drug dispensers, to evaluate pharmacist provision of emergency contraception and to investigate consultation quality at community pharmacies.

In a descriptive cross-sectional study of Tanzania, mystery shoppers visited 206 private pharmacies with prescriptions for Artemether-Lumefantrine, Amoxycillin and Metronidazole. To assess dispensing skills of drug dispensers, a checklist was used by simulated patients and 186 were directly interviewed using structured questionnaires and Focus Group Discussions (FGDs) to assess their knowledge of dispensing. Among 206 pharmacies, there were only 29.6% of trained pharmaceutical personnel and the rest 70.4% were non-pharmaceutical personnel. The dispensing skills of drug dispensers showed a range between 25.7% and 70.4% and their knowledge of dispensing had percentage ranges of only 11.4% (low) to 83.2% (medium) levels. This study suggested that prescription only medicines should be

dispensed by well-trained pharmaceutical staff and capacity building of drug dispensers should also be improved (65).

The evaluation of pharmacist provision for emergency contraception pill (ECP) by using secret shoppers includes 5 trained secret shoppers and 34 pharmacies were visited to request ECP. The secret shoppers were trained for role playing and familiarization with ECP taking two hours. They were also provided with one of two scripts about appropriateness of ECP. They were also asked to assess answers to specific closed questions, give comments about the visiting time, their perception about pharmacists and the degree of privacy at the pharmacy. Most pharmacists followed the protocol correctly in scenarios of script one and 71.4% of pharmacists provided alternatives to ECP in script two. The shoppers only gave negative comments concerning with privacy at the pharmacy. This study concluded that the use of secret shopper permitted assessment of pharmacist-customer interaction to provide necessary feedback on some areas such as more training for pharmacists may be required (66).

A study conducted by repeated secret shopping as a form of audit and feedback in community pharmacies in Australia concluded that the management of community pharmacy for non-prescription medicine requests could be improved by repeated secret shopping. Sixty-one undergraduate secret shoppers made over nine visits and the total visits for 36 different community pharmacies was 540. After analyzing 521 visits, 54% of them showed an appropriate patient outcome and thus

the predictors of a visit may involve repeated visits, involvement of pharmacist, increased questioning, and the prescribed scenario (67). The willingness to give consultation could also be observed in pharmacy staff (83%) and the relation between the consultation quality and pharmacy profession and pharmacy size were also evaluated by the use of mystery shopper studies which may give valuable information for training schemes (68).

In Myanmar, mystery client survey at community pharmacies was also made in Yangon region. The drugs of interest were antibiotics and performed mystery client survey using 5 case scenarios in 8 pharmacies to evaluate dispensing practice of drug sellers. The antibiotics included in this survey were Amoxicillin, Cotrimoxazole, Erythromycin, Metronidazole, Tinidazole, Ciprofloxacin, Norfloxacin and Neomycin. In this mystery client survey, all pharmacies sold antibiotics when customers need it. A total of 144 registered pharmacies were also included for face to face interview and among them, only 4.9 % have trained pharmacists who could gave right drug information about antibiotics for the questionnaires. This study suggested that there should be strengthening of law and policy for antibiotic prescription and making advocacy and training programs for drug sellers about antibiotics usage (22).

In conclusion, many countries especially low- and middle-income countries had insufficient pharmacist workforces and there was little number of pharmacists on duty in the community pharmacies. Many consumers did not get enough drug information and relevant dispensing services from the dispensers of community

pharmacies and most of them were not even asked for their disease history to check whether they got appropriate drug treatments. Therefore, they might need additional drug information to use their drugs safely and appropriately.

2.4.3. Review and comparison of different PIL guidelines

The guidance on how to create well-designed leaflets has been developed in some countries, but only a few of them have the enforcement to include leaflets for the patients along with the medicines. The research conducted on the comparison of recommendations made by Raynor et al. and different regulatory agencies' recommendations for medicine information leaflets used 20 good-design principles created by the researchers. They selected guidelines which were available freely online in English from the EU, New Zealand, the UK and the USA. There was variation of design recommendations for medicine information leaflets among the regulatory agencies and the guidelines were not in line with the researchers' 20 good-design principles. Table 1 shows examples of design principles that compared in this study. Similarities were found among the guidelines of the EU, the UK and the USA. They suggested to provide up-to-date and enforceable guidance for creators of medicine information leaflets to an appropriate standard (69).

The international perspectives on consumer medicine information compared strength and weakness of legislations across three continents: the US, the EU countries and Australia. In Australia, CMIs need to be available with all new

medicines and are written by the manufacturer and the contents of which need to be consistent with the Product Information (PI) according to the Therapeutic Goods Act. The voluntary provision of package insert leaflets for patients was started to apply in the US and the supply of hard copy or computer-generated medication guides with every prescription must also be produced and supplied by the manufacturers. However, in the EU, the legislation related to CMIs was introduced in the 1990's and forced to supply information inside the pack of every medicine according to the EC directive 92/27 and after that the readability guideline for leaflet was also published (70).

The other study performed on the comparison of international guidelines on written medicine information (WMI) only described the current government regulations, guidelines and recommendations of WMI only in the EU, the USA and Australia. In this review, the researchers extracted and described the target audience, legislative guidance, design/ format, legislative schedules, content, writer, evaluators and other guidance for SmPC and PI/PIL in those three regions. They concluded that the EU had a stronger organized regulations and guidance, while the US seemed to have a moderate one and Australia appeared to have a weaker regulation. Although the detailed contents varied, the pharmaceutical companies in all three regions must follow the legislations and guidelines set out by the respective DRAs (71). The following shows an example of comparison showing WMI regulation in the EU.

2.5. Current situation of Pharmaceutical Regulations and Drug Product Information in Myanmar

2.5.1. Healthcare services and drug availability

Since Myanmar had been struggling with political, socioeconomic and civil unrest after its independence, the World Health Organization (WHO) ranking for Myanmar revealed remarkedly low in overall health systems globally (72). While looking at healthcare, several problems related to quality of healthcare services, nutrition, maternal and child health, infectious disease controls, and access to healthcare services are still occurring (73). Government has the primary role of providing healthcare and numbers of public hospitals have been significantly improved and much more government budget has been allocated for healthcare sectors. However, government hospitals are still lacking sufficient funds and shortage of medicines and thus allocation of more funds are needed. The urban areas like Yangon and Mandalay were receiving more funds from the government. The healthcare services are more accessible to urban areas than rural areas and access to specialty services is challengeable to both urban and rural areas (74).

Although health insurance system is not too much developed in Myanmar, most of the essential medicines are provided by the government hospitals free of charge. If the medicines are not available from the government hospital, patients have to buy themselves deploying out-of-pocket payment systems. Therefore, government cannot provide all drugs and people have to buy their drugs from the

private pharmacies. In 2014, the out-of-pocket payment in Myanmar was 51% of health expenditure (21). In addition, only 31.4% of population lives in urban areas and pharmacies are not located in the rural areas. Outside of the city hospitals, rural health centers (RHCs) and sub-RHCs are often limited to providing essential medicines. Most of these centers from rural areas typically suffer from shortage of doctors and are often headed by poorly trained health supervisors who can only perform basic treatments. These centers also refer patients to nearby hospitals for more advanced treatment. Patients have encountered unnecessary death because of lack of adequate medicine supply nearby areas (74).

In 2016, Myanmar had 1056 public hospitals and these facilities mainly provide curative and rehabilitative services. Among these hospitals, there were 4 general hospitals with up to 2000 beds, 50 specialist/teaching hospitals with 100-1200 beds, 55 regional/state/district hospitals with 200-500 beds, 330 township hospitals with 25-100 beds and the remaining 617 hospitals were station hospitals with 16- 25 beds. The other types of public health facilities were 2199 preventative and public health services and 259 traditional medicine facilities (75). Myanmar has health expenditure of 2.3%of GDP which is lower than WHO recommendation and the government spends only 3-5% of healthcare budget on medical goods and a larger share was given to health-related functions. Although expenditures on medicine has increased from 2 to 3 USD/person/year, baseline survey of the national

supply chain in 2013 showed that 56% of facilities experienced stock-outs of medicines (74).

There were only 8 government pharmaceutical manufacturers for allopathic medicines and 3 private manufacturers in Myanmar. About 17,000 allopathic products are imported by 170 importers and thus only 20-30% of the essential drugs are available from the domestic manufacturers (74). Thus, most of the drugs are imported from other countries and the labels of these products are only available in English language either when registered or distributed around the country. Since Myanmar has adult (15 years and older) literacy rate of 75.55% and health literacy of about 31.5%, it is not sure that patients can read and understand English labels and leaflets for professionals provided along with the medicines (76, 77).

The requirement for healthcare services in Myanmar is varied from primary healthcare with free medication emergency medical services and the provision of information about the medications is the fundamental responsibility of all healthcare professionals. However, in a time limited environment, there is insufficient time for advising patients. In Myanmar, the delivery of outreach and static health services are impeded by shortage and misdistribution of health workforce, lack of essential medicines, infrastructure and allowances. The ratio of health workforce per 1000 population is also lower than WHO recommendation (1.47 per 1000 population) and the distribution of them were not even around the country. Moreover, there were

only 2553 pharmacists which is not sufficient to be employed as community pharmacists and thus most of the pharmacy shops do not have pharmacists (78).

Health services provided by pharmacists especially in public hospitals are very limited in Myanmar. The roles and responsibilities of most hospital pharmacists are inventory function and only few pharmacists have dispensing functions. The compounders who have one-year training or paramedical staffs are generally doing dispensing in the outpatient department (OPD) pharmacies of public facilities. There is insufficient time for dispenser to educate patients on how to take their medicines, because the patient-dispenser time was often less than one minute. In most of the private pharmacies, dispensing is done by unqualified staff and supervised by a shop-owner who has some kind of graduate qualification but not one in pharmacy (74).

2.5.2. Licensing of drugs and community pharmacies

Although Myanmar has the National Drug Law, it does not describe specifically about the drug schedules. However, in general, there are three main drug schedules namely Over the Counter (OTC), Prescription only Medicine (POM) and Controlled Medicine which is subdivided into highly and limited controlled medicines. According to 1992 Drug Law, Myanmar Food and Drug Board of Authority was formed and its functions and duties included laying down the polices, determining, stipulating, permitting or refusing relating to registration of food and drugs, terms and conditions of food and drugs and forming state and region Food

and Drug Supervisory Committees in the states, divisions, districts and townships to supervise matters related to food and drugs (79).

For the licensing process of drugs, the key regulatory procedures include product dossier evaluation, registration of drugs, checking the samples for Quality Control testing and medical product recall or withdrawal are mainly performed by the Central Food and Drug Administration in Nay Pyi Taw to give approval for product registration and importation certificates. The pharmaceutical companies have to renew their registration certificate for each dug every five years and importation certificate for every three years.

The other decentralized processes are inspection of drug outlets, participation in the State and Regional Food and Drug Supervisory Committees and post marketing sampling. The inspection of drug stores is delegated to the Food and Drug Supervisory Committees at district and township level and the chairperson of the committee at township level is township hospital medical superintendent. Therefore, the issuance of licenses and regulatory inspection for drug outlets or community pharmacies is delegated to the Food and Drug Supervisory Committees at district and township level, which are supervised by similar committees at State and Regional levels. The lifetime of license for a pharmacy is 3 years and at least one inspection is needed for the renewal process. If a pharmacy has this type of license, they can only sell OTC and POM with or without prescription. For the pharmacy where controlled drugs are sold, a physician's prescription and signature

are needed to sell a controlled drug and the license must also be renewed annually (74).

2.5.3. Availability of drug product information

The drugs manufactured locally or imported into Myanmar have been regulated by Department of Food and Drug Administration. The reviews of all specifications for registration process or marketing authorization have been required according to ASEAN guidelines. However, the outer package, container, bottle, blister and inner package inserts for professional use can be described in only Myanmar language or English or both as mentioned in Regulations on Drug Law, order 7/93 (24). The requirements for the provision of leaflets for consumers were not described in any regulations and thus patients could not get any drug information leaflets other than that provided by dispensers from OPD pharmacies of private hospitals or private pharmacies.

The contents of carton box and leaflets described in labelling requirements of order 7/93 are as follows:

Carton Box

1. Brand Name
2. Generic Name
3. Standard (USP, BP....)
4. Active Ingredient
5. Batch Number
6. Manufactured Date

7. Expired Date
8. Pack Size
9. Name and Address of Manufacturer
10. MM Registration Number
11. Method of Administration
12. Storage Condition
13. Prescription Only Medicine (if it is not OTC)
14. Veterinary Use Only (if for animals)
15. Precautions

Leaflets:

1. Brand Name
2. Generic Name
3. Active Ingredient (also amount)
4. Pharmacological Actions
5. Indications
6. Adverse Reactions
7. Contraindications
8. Drug Interactions
9. Precautions
10. Dosage
11. Storage Conditions
12. MM. Registration Number
13. Name of Address of Manufacturer

The dispensing by pharmacists or compounders could be observed at pharmacy counters, the interaction time or discussion time between them are less than one minute and no labelling is observed except writing number of tablets and frequency per day on the strip packing. Almost all of the private pharmacies do not

employ pharmacists and thus the dispensing process are often done by unqualified staff and supervised by a shop-owner. Moreover, some medicines are stored in sub-optimal conditions and which do not comply with good pharmacy practice (GPP). About half of the customers who came to those pharmacies carried their patient records for administration, but some did not have (74).

A range of sources of medicine information for patients, caregivers and users of medicines are available to the public. These include verbal information from health care professionals, written information such as medicines labelling and information leaflets or package inserts which are supplied with individual medicines, written information available from patient or health care professional organizations, governmental and non-governmental health organizations, pharmaceutical companies and other organizations that communicate with patients, websites that provide information on medicines or health conditions, digital resources such as mobile health apps and social media (80). However, in Myanmar, the availability of drug information from independent sources is also limited. Not too many people are using internet to search information about their medications. Although Master Index of Medical Specialties (MIMS) has been published locally, information provided by medical representatives is available only for medical practitioners.

CHAPTER III- METHODOLOGY

This chapter includes the methodologies which were applied for the study to fulfil the research objectives.

The current situation of providing medication information to Myanmar people was assessed by collecting drug information attached with drug products and by performing simulated-patients method. Shopping as a simulated patient was made at community pharmacies and the drug information provided by dispensers who may be pharmacists or non-medical professionals were evaluated.

Additionally, the targeted review of the literatures was also investigated to identify which countries had been implementing PILs regulations. The resulted regulations and guidelines of PILs were reviewed and compared in terms of drugs required PILs, designs, designs, contents and user-testing across various DRAs.

3.1. Evaluation of drug information available for Myanmar consumers

The objective I is to evaluate drug information provision for Myanmar people which includes two phases. The first phase is the assessment of drug information attached with the drug products and the other is the assessment of drug information services at community pharmacies by using simulated- patient method.

3.1.1. Evaluation of drug information attached with drug products

I. Study design

It was aimed to evaluate the information provided along with drug products in each drug category and thus content analysis was conducted.

II. Drugs of interest

In Myanmar, there are three main drug categories: over the counter medicine (OTC), prescription only medicine (POM) and controlled medicine (highly and limited). All three drug categories were included for this evaluation. Ten drugs for each category were selected according to two criteria: top market share drugs and most dispensing drugs (81).

Table 3.1 List of drugs for each drug category

Drug category	Drug product (Brand name)	
OTC	Normagut Capsule	Air-X Tablet
	Enervon-C Tablet	Oramin-G capsule
	Ferro-denk 50 Tablet	Livolin Forte Capsule
	Vitamin E 400 IU Capsule	Pepsol Capsule
	Facia Capsule	Konimag Suspension
POM	KBN Amoxicillin Capsule	Bluecap Capsule
	Telsafe-40mg Tablet	Naclo-R Capsule
	Pacfen 200 Tablet	Monotrate 20 Tablet
	Panfor-SR 500 Tablet	Vastarel MR Tablet
	Banzatin Tablet	Diamicron MR 60mg Tablet

Controlled medicine	Xanax 0.25 mg Tablet	Naze-1 Tablet
	Easium Tablet	Milam 7.5mg Tablet
	Frixitas 0.5mg Tablet	Sedil Tablet
	MST Continus 30mg Tablet	Ultracet Tablet
	Nitee-5 Tablet	Tramalin-100 Capsule

III. Data extraction

The contents of information provided in the carton box and leaflets of 30 drug samples were extracted based on three domains:

- Language use (e.g. local, English or other language)
- Information format (e.g. font type and size)
- Information topics (e.g. drug name, indication, dosage and drug administration etc.)

After the data were extracted, content analysis was used for data analysis by the main researcher. For the characteristics of carton boxes and leaflets, the language, targeted reader, font type and size were identified and grouped into the same topics. After that the available contents of drug information were extracted and checked whether these were complied with the labelling requirements of Regulations on National Drug Law 1992. The extracted data were also verified by two reviewers for the validity of content analysis.

3.1.2. Evaluation of verbal and written drug information provided by drug dispensers

This part of study focused to evaluate both verbal and written drug information provided while medicines were dispensed in community pharmacies. In this study, community pharmacy was defined as a retailed pharmacy shop which is registered at township level Food and Drug Supervisory Committee of Yangon Region.

I. Study design

Standardized simulated patient survey was carried out during November to December 2019 to assess drug information provided at the point of dispensing in community pharmacies. Verbal and written drug information was collected in this study. Three trained simulated patients and the main researcher were in the field visiting community pharmacies of selected townships in Yangon region.

II. Scope of the study

Yangon region was selected as a study site as it is a commercial capital with highest population density and highest pharmaceutical market value (82).

III. Sample size calculation

Although the township is the sampling unit, the community pharmacy is an element to be studied. Sample size was calculated to ensure the minimum numbers

of pharmacies to be included for accuracy of parameter estimate. Sample size formula for mean estimate with finite population was used.

$$\text{Sample size, n} = \frac{N{Z^2}_{\alpha/2}\,\sigma^2}{Ne^2 + {Z^2}_{\alpha/2}\,\sigma^2}$$

N = 5,600 pharmacies (based on Yangon FDA data as of September 2019)

$Z_{\alpha/2}$ =1.96

σ = 0.17 (obtained from previous study (83))

e = 0.02

The sample size needed was 264 community pharmacies in this study.

IV. Sampling method

The sampling method was stratified, single-stage cluster sampling because the population density and urbanization are different among the townships of interested population. In Yangon, there are 4 districts composed of 45 townships (84). All townships were stratified into 6 strata by population density as shown in Appendix I.

One township from each stratum was randomly selected to increase representativeness of the sample from all 6 strata. All pharmacies from selected townships: Pabedan Township, Pazundaung Township, Lanmadaw Township, Dawbon Township, Botahtaung Township and Hmawbi Township were included in this survey.

V. Case preparation and standardization of simulated patients

In order to assess both verbal and written information provided by staffs who could be pharmacists or non-pharmacists, case preparation and standardization of simulated patients need to be prepared.

A. Selection of drug

Among three main drug classes in Myanmar, only OTC medicines can be advertised in any types of media and consumers usually buy themselves from the community pharmacies for their minor health problems. Although, there has not been proper audit of the market, OTC medicines contribute to the highest market share. Among OTC medicines, non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used and Mefenamic Acid was included in the list of top 20 products (82). Also, it needs some special precautions before taking medicines. For these reasons, Mefenamic Acid 250mg Tablet was selected as the tracer drug for simulated-patient survey.

B. Simulated patients

There were four simulated patients: main researcher and three requested pharmacists. They were trained and rehearsed with the use of scenario to find the problems which may be encountered during real practice and to standardize the process of shopping as a simulated patient. They were also instructed not to initiate any questions regarding the purchased drug. But they would ask “how should I take

and how long should I take this medicine' if dispensers did not provide any information about the drug. All the collected data will be recorded in google documents after each shopping. No audio recording was used during data collection since only request letters were sent to the respective Township level Food and Drug Supervisory Committee.

C. Scenario for simulated patients

A woman with the age of 20-30 years old entered a pharmacy and asked for Mefenamic Acid 250mg Tablet. The untold background of this patient was that she was suffering from symptoms of dysmenorrhea. Her menstrual history was normal. She had never had gastritis or stomach pain and not allergic to any kind of analgesics. She had not been using any other kinds of drugs in her daily life.

VI. Assessment of drug Information services

The following activities were assessed for the evaluation of providing drug information services.

1. Illness and medical history taking assessment
2. Provision of verbal drug information
3. Provision of written drug information

To evaluate these three activities, the indicators were set up by using the leaflets for Mefenamic Acid approved by Myanmar FDA and the previous study on the assessment of dispensing practices in community pharmacies (82). The scores for

each activity were determined based on their clinical importance. All measurements were given 1 score each except for the important and necessary information such as precautions, dosage and administration which were given 2 scores. The measurement indicators were also validated by interviewing a senior pharmacist from Myanmar FDA and an expert from clinical field.

The scores and measurements used for each drug information service activity were shown in Table 3.2. The maximum score is 18 points for the assessment of drug information service scores.

Table 3.2 Scores and measurements used for each activity

Activity	Measurements (Indicators) (18 points)	Score
1. History Taking	a) Asking about symptoms to ensure that the requested drug is appropriate	1
	b) Asking about history of gastritis or Gastroesophageal Reflux Disease (GERD)	1
	c) Asking about history of allergic to Mefenamic Acid	1
2. Verbal Drug Information	a) Name of medication (brand name or generic)	1
	b) Take 1-2 tablets every 8 hours	2
	c) Take the medicine immediately after meals	2
	d) Stop taking medicine if symptoms disappear	2
	e) Should not concomitantly use other NSAIDs	1
	f) Common side effects (abdominal pain, diarrhea, skin rash)	1
3. Written Drug Information	a) Name of medication (brand name or generic)	1
	b) Take 1-2 tablets every 8 hours	2

	c) Take the medicine immediately after meals	2
	d) Should not concomitantly use other NSAIDs	1

The characteristics of pharmacies including qualification of dispensers and number of consumers in the pharmacy were also recorded during survey. The dispensers' qualification was identified by observing their white coats, identity cards and the pharmacy's licenses describing the qualification of authorized dispensers.

The information service scores for each activity and scores for overall drug information services were assessed. Subgroup analysis was also evaluated for the pharmacies' characteristics.

VII. Statistical analysis

Descriptive statistics was used to report in terms of percentage and mean. To compare providing each part of drug information service, Fisher's exact test was used since the expected frequency counts were less than 5 to determine differences in providing information of each measurement. Independent T-test was used to identify differences in mean scores of each activity and to analyze the association between mean scores of drug information services and characteristics of pharmacies. The results were considered statistically significant if p-value was less than 0.05.

3.2. Targeted literature review on international PIL development guidelines

The main study design for objective II was targeted review of the literatures which helped to analyze the regulations and guidelines of PILs and to know how PILs are developed across various countries.

3.2.1. Search strategy

A systematic literature search was conducted on Google by using the combination of the search terms 'patient information leaflet' or its synonyms and the name of 218 countries from the World Bank list of countries (85) as shown in Appendix II. The search was also limited to the online articles which were available prior to April 2019. From this searching, the names of countries which had been implementing PILs were observed.

3.2.2. Data collection and analysis

The DRAs websites of all 218 countries were also explored to ensure that countries which have PILs regulations and guidelines are included in this study. Regulations and guidelines that could not be translated into English will be excluded from the study. The identified regulations and guidelines were extracted by one reviewer using a data extraction form. The extracted data were divided among other two reviewers for data verification. The collected data were analyzed using content analysis to review and compare designs, contents and user-testing of PIL guidelines across various countries and groups of countries.

3.3. Ethical considerations

The study was approved by thesis committee of the Department of Social and Administrative Pharmacy from the Faculty of Pharmaceutical Sciences, Chulalongkorn University.

The study was also be reviewed by the Ethics Review Committee of Department of Food and Drug Administration, Ministry of Health and Sports, Myanmar. The required data were collected from all the community pharmacies of selected townships. The pharmacy owners were not be informed about the survey since individual data and characteristics of the pharmacy staffs and name of pharmacies involved will not be disclosed in the results to protect their privacies.

CHAPTER IV- RESULTS

This research had evaluated current situation of how much Myanmar consumers got drug information in which the data was collected by content analysis and simulated patient survey method. In addition, the international guidelines of PILs concern designs, contents and user testing with the application of targeted literature review as a main method.

This chapter presents findings of the research data and presentations of results are divided into two parts on the basis of research objectives as follows:

1. Evaluation of drug product information provision for Myanmar consumers
2. Targeted literature review on international PIL development guidelines

4.1. Evaluation of drug product information provision for Myanmar consumers

4.1.1. Evaluation of drug information attached with the drug products

Table 4.1 represents that the majority of both carton boxes (83.3%) and leaflets (86.7%) were available in English language and there was only one leaflet described in both English and Myanmar languages. The contents included in the leaflets were intended to for healthcare professionals use in 86.7 % of drugs and only 6.7% of drugs had leaflets which were understandable for consumers whereas the remaining drugs had leaflets with contents for both healthcare professionals and

consumers. But all the drugs described contents for consumers on their carton boxes.

Most commonly used font types and sizes used for carton boxes were Helvetica 12 and PT serif 12 which were found in 30% and 16.7 % of drugs respectively. In the leaflets, there were various types of font sizes and types including Myanmar 3 font which was found only in one drug. The most commonly used font was Times News Roman 10 and other fonts including Arial 10, Helvetica 8, Mukta 10 and Tahoma 10 showed equal number of 10 %.

Table 4.1 General characteristics of carton box and leaflets of 30 studied drugs

Characteristics	Carton Box n (%)	Leaflet n (%)
Language		
English only	25 (83.3)	26 (86.7)
Both Myanmar and English	0	1 (3.3)
English and Other Languages	5 (16.7)	3 (10)
Targeted Reader		
For Healthcare Professionals	0	26 (86.7)
For Consumers	30 (100)	2 (6.7)
For Healthcare Professionals and Consumers	0	2 (6.7)
Font Size and Type		
Arial 10 (Arial 10)	0	3 (10)
Arial 12 (Arial 12)	4 (13.3)	1 (3.3)
Helvetica 8 (Helvetica 8)	0	3 (10)
Helvetica 10 (Helvetica 10)	3 (10)	2 (6.7)
Helvetica 12 (Helvetica 12)	9	2 (6.7)
Mukta 10 (Mukta 10)	0	3 (10)
Mukta 12 (Mukta 12)	0	2 (6.7)

Tahoma 10 (**Tahoma 10**)	3 (10)	3 (10)
Times New Roman 9 (Times New Roman 9)	0	2 (6.7)
Times New Roman 10 (**Times New Roman 10**)	4 (13.3)	4 (13.3)
Times New Roman 12 (**Times New Roman 12**)	1 (3.3)	2 (6.7)
PT Serif 10 (PT Serif 10)	1 (3.3)	2 (6.7)
PT Serif 12 (**PT Serif 12**)	5 (16.7)	1 (3.3)
Myanmar 3 9 (မြန်မာ ၃ ၉)	0	1 (3.3)

Table 4.2 Contents of carton boxes and leaflets in each drug class

Contents	OTC (n=10)		POM (n=10)		Controlled (10)	
	Carton Box n (%)	Leaflet n (%)	Carton Box n (%)	Leaflet n (%)	Carton Box n (%)	Leaflet n (%)
Brand name	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**
Active ingredient	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**
Dosage form	5 (50)	4 (40)	10 (100)	10 (100)	10 (100)	8 (80)
Inactive ingredient	1 (10)	4 (40)	1 (10)	5 (50)	0	3 (30)
Indications	5 (50)	**10 (100)**	2 (20)	**10 (100)**	1 (10)	**10 (100)**
Dosage and Administration	8 (80)	**9 (90)**	2 (20)	**9 (90)**	3 (30)	**10 (100)**
Warnings and Precautions	**0**	**7 (70)**	**1 (10)**	**8 (80)**	**1 (10)**	**9 (90)**
Pack size	**10 (100)**	9 (90)	**10 (100)**	10 (100)	**10 (100)**	7 (70)
Local registration number	**10 (100)**	**0**	**10 (100)**	**4 (40)**	**9 (90)**	**0**
Foreign registration number	5 (50)	1 (10)	0	0	2 (20)	0
Storage conditions	**10 (100)**	**7 (70)**	**10 (100)**	**10 (100)**	**10 (100)**	**9 (90)**
Manufacturer	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**	**10 (100)**
Distributer	3 (30)	2 (20)	2 (20)	1 (10)	3 (30)	3 (30)
Manufactured date	**10 (100)**	0	**10 (100)**	0	**10 (100)**	0
Expired date	**10 (100)**	0	**10 (100)**	0	**10 (100)**	0
Batch number	**10 (100)**	0	**10 (100)**	0	**10 (100)**	0
Pharmacopoeia standards	**3 (30)**	0	**5 (50)**	0	**5 (50)**	0
Physical appearance	0	1 (10)	0	4 (40)	0	5 (50)
Contraindications	0	**7 (70)**	0	**8 (80)**	0	**10 (100)**
Pharmacological action	0	**5 (50)**	0	**4 (40)**	0	**7 (70)**
Pharmacokinetics	0	3 (30)	0	6 (60)	0	5 (50)
Pregnancy and lactation	0	4 (40)	0	2 (20)	0	8 (80)
Drug interactions	0	**4 (40)**	0	**7 (70)**	0	**8 (80)**
Adverse reactions	0	**6 (60)**	0	**10 (100)**	0	**10 (100)**
Overdosage	0	4 (40)	0	5 (50)	0	5 (50)

Note**: Bold fonts** = required information according to Regulations on National Drug Law

For the contents in carton boxes and leaflets were demonstrated and classified on the basis of 30 drug products for 3 drug categories as shown in Table 4.2.The results of carton box contents represented that essential contents required by law: “brand name”, “generic name/active ingredient”, “pack size”, “storage conditions”, “manufacturer”, “manufactured date”, “expired date” and “batch number” were included in all drug categories. However, 90 % of controlled drugs contained “local registration number” on the carton box while the “pharmacopeia standards” were found only in 30% of OTC drugs, 50% of both POM and controlled drugs despite they need to provide according to law. Additionally, the other information such as “indications” and “distributer” were observed in some drug categories.

Although the carton boxes of almost all drugs had mandatory contents, the study showed that the leaflet contents were not found to have all. The most commonly contents like “brand name, “generic name/active ingredient”, “indications” and “manufacturer” were found in all drug categories. But essential contents such as “contraindication” were not provided in all drug categories. The “local registration number” was not also provided in the leaflets of all OTC and controlled drugs while only 40 % of POM drug leaflets and 90% of controlled drug leaflets described it. The other specific information such as discontinuation of therapy for controlled drugs was only found in leaflet of one drug.

4.1.2. Evaluation of verbal and written drug information provided by drug dispensers

Table 4.3 Baseline information about pharmacies that could influence drug information services

Characteristics	Frequency (%)
Dispensers	
Pharmacist	9 (3.6)
Non-pharmacist	238 (96.4)
Number of consumers	
0-3 consumers	211 (85.5)
>3 consumers	36 (14.5)

After 4 simulated patients visited all pharmacies in 6 selected townships of Yangon region, only 247 pharmacies were found for this study. The result from table 4.3 shows the baseline information about pharmacies which were visited by simulated patients. Out of 247 pharmacies, there were only 9 pharmacies (3.6%) which had pharmacists on duty and the rest 96% of drug dispenser were non-pharmacists. During the visits, only 14.5% of pharmacies were crowded with other clients which were more than 3 consumers while the majority of pharmacies (85.5%) had a few numbers of consumers (0-3).

Table 4.4 Descriptive statistics of providing drug information services

Activity (Measurements)	Pharmacist (n=9) n (%)	Non-pharmacist (n=238) n (%)	p-value
History taking			
1. Asking about symptoms to ensure that the requested drug is appropriate	1 (11.1)	18 (7.6)	0.519
2. Asking about history of gastritis or GERD	0	4 (1.7)	0.861
3. Asking about history of allergic to Mefenamic Acid	0	0	-
Verbal drug information			
1. Name of medication (Mefenamic Acid or Specific Brand Name)	0	0	-
2. Take 1 to 2 tablets every 8 hours	9 (100)	230 (96.6)	0.740
3. Take the medicine immediately after meals	8 (88.9)	156 (65.5)	0.135
4. Stop taking medicine if symptoms disappear	0	26 (10.9)	-
5. Should not concomitantly use other NSAIDs	0	0	-
6. Common side effects (abdominal pain, diarrhea, skin rash)	0	1 (0.4)	-
Written drug information			
1. Name of medication (Mefenamic Acid or Specific Brand Name)	0	0	-
2. Take 1-2 tablets every 8 hours	3 (33.3)	110 (46.2)	0.341
3. Take the medicine immediately after meals	3 (33.3)	34 (14.3)	0.137
4. Should not concomitantly use other NSAIDs	0	0	-

Note: p-value for all comparisons were not significant

The results from this table showed the comparison of frequency and percentage of each measurement for drug information services which were provided by pharmacists and non-pharmacist during simulated patient visit.

The research reported that there were three main activities which included 13 indicators to measure drug information services and information for each measurement was analyzed by deciding whether they were provided by dispensers or not. Most dispensers, 9 pharmacists (100%) and 230 (96.6%), provided verbal dosage information (1 to 2 tablets 8 hourly should be taken) and written dosage information was provided by 33.3% (n=3) of pharmacists and 46.2% (n=110) of non-pharmacists. The warning to take the medicines immediately after meals was given orally by 88.9% of pharmacists and 65.5% of non-pharmacists. The researcher got verbal information about common side effects of drugs from 1 dispenser who was non-pharmacist. But asking patients whether patients has allergic to Mefenamic Acid and both verbal and written information about medication name and concomitant use of other NSAIDs were not provided by the dispensers from all pharmacies.

On the other hand, Fischer's exact test was used to compare the information provided by pharmacists and non-pharmacists. However, statistically significant differences were not found among all information service activities.

Table 4.5 Mean score differences for drug information services of each activity provided by dispensers

Activity	Mean scores (±SD) for both dispensers (n=247)	Mean scores (±SD)		
		Pharmacist (n=9)	Non-pharmacist (n=238)	p-value
History Taking (score range, 0-3)	0.09±0.305	0.11±0.333	0.09±0.304	0.737
Verbal drug information (score range, 0-9)	3.11± 1.556	3.11±1.453	3.11±1.562	2.95±1.224 0.246
Written drug information (score range 0-6)	1.05±1.335	1.33±2.00	1.04±1.308	0.002*
Total mean scores for all services (score range, 0-18)	4.25±2.062	4.56±2.877	4.24±2.033	0.082

*p-value<0.05 (statistically significant)

According to the objective of this research, the drug information provision was evaluated to check how much Myanmar consumers can get from the dispensers. But Independent T-test was also used to compare mean score differences between pharmacists and non-pharmacists. The results for the Student T-test and Welch T-test still showed no significant difference between pharmacist and non-pharmacists except for providing written drug information.

Table 4.5 showed that the mean scores and differences in mean scores of drug information services provided by pharmacists and non-pharmacists compared by Independent T-test. Regarding the general results of drug information services for both types of drug dispensers, it was found that mean scores for history taking activity was 0.09±0.305 (score range was 0-3) and consumers were not asked about their disease history to ensure safe use of drugs. The results revealed that the mean scores for verbal and written drug information were 3.11±1.556 and 1.05±1.335 respectively. The dispensers intended to provide verbal drug information mostly in a correct way among other activities. The total mean score of drug information services (maximum score = 18) was 4.25±2.062 and it was proved that only a few information for Mefenamic Acid were available for consumers.

The results Independent T-test represented that the mean scores comparison for history taking and written drug information were not statistically among pharmacists and non-pharmacists. However, the mean scores for written drug information provided by pharmacists were statistically higher than that provided by non-pharmacists.

Table 4.6 Comparison of overall drug information service scores for different characteristics of pharmacies

Characteristics (N=247)	Frequency	Mean of Drug Information Scores	SD	t-value	p-value
Dispensers					
Pharmacist	9	4.56	2.88	-.451	0.082
Non-pharmacist	238	4.24	2.03		
Number of Consumers					
0-3 consumers	211	4.34	2.01	1.670	0.353
>3 consumers	36	3.72	2.30		

Note: p-values were not statistically significant.

As presented in table 4.6, the subgroup analysis of dispensers' qualification and number of consumers in pharmacies were performed. Among 247 pharmacies, there was difference in mean scores of overall drug information services provided by pharmacists and non-pharmacist dispensers, but statistically not significant, t (245) = -.451, p-value = 0.082. Interestingly, the dispensers provided more drug information when there were a few consumers (4.34±2.01) in the pharmacies although statistically not significant, t (245) = 1.670, p-value = 0.353.

4.2. Targeted literature review on international PIL development guidelines

According the list of countries from the World bank, there is 218 countries in total. The literature search on Google was performed with the combination of search

term ‘patient information leaflet’ or its synonyms with the name of countries from World Bank List.

The findings of this study showed that 69 countries and 3 groups of countries which were interested in the implementation of PILs. Regarding the search on all DRA websites, it was found that about 11% of 218 countries around the world were conducting only researches that were related to PILs including patients’ perception about PILs reading or user testing. There were only 9 countries (about 4.13%) had their own guidelines.

Additionally, the researcher also found that 3 groups of countries (international organizations) had guidelines for their member countries. Among these 3 organizations, EU and GCC had respective DRA for their own member countries and ASEAN does not have.

Figure 1 demonstrated that the world map showing 20.6% of countries had guidelines to create PILs in their countries and the rest 79.4 % were not enforcing to use PILs in their countries. The overall results showed that there was a total of 12 PILs guidelines for the review and comparison in this study.

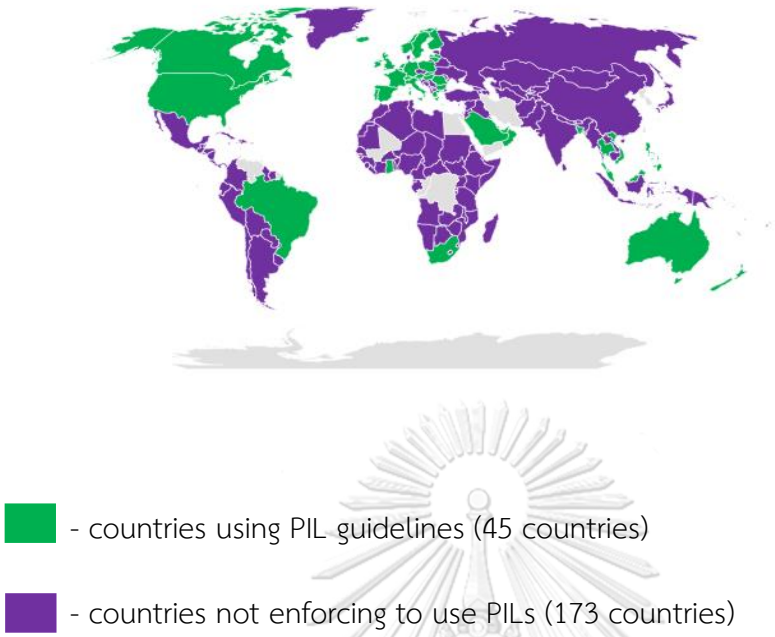

Fig. 4.1 World map showing countries on implementation and guidelines of PILs

Among 218 countries from World Bank List, 45 countries were enforcing the implementation of PILs and were using guidelines to create PILs whether they had their own guidelines or not. Out of 45 countries, only 20% of them had their own guidelines and the names of countries were Australia, Brazil, Canada, Malaysia, New Zealand, South Africa and Thailand. Besides, the EU and the Gulf Cooperation Council had developed common PIL guidelines for their member countries and ACTD guideline mentioned only the contents of PILs. The rest 80% had been using the guidelines of their organizations or adopting other countries' guidelines.

4.2.1. General information about 12 PIL guidelines

The DRA websites of all regions were looked through to find their PILs guidelines except ASEAN since it does not have specific websites for drug regulatory considerations of their own. The guidelines of all DRAs were published online on their websites and ACTD was found through ASEAN website (https://asean.org/).

Figure 4.2 demonstrated that timeline for the latest edition and available languages of guidelines. Almost all PILs guidelines were also available in English language except Brazil, Malaysia and Thailand since these three countries used their official languages (86-88). Besides, the design and contents of Malaysian guidelines were described both in Bahasa Malaysia and English languages. The results represented that the most updated guideline was from Malaysia which was published in 2019 and the oldest ones were from Australia and USA in 2006 (19, 87, 89).

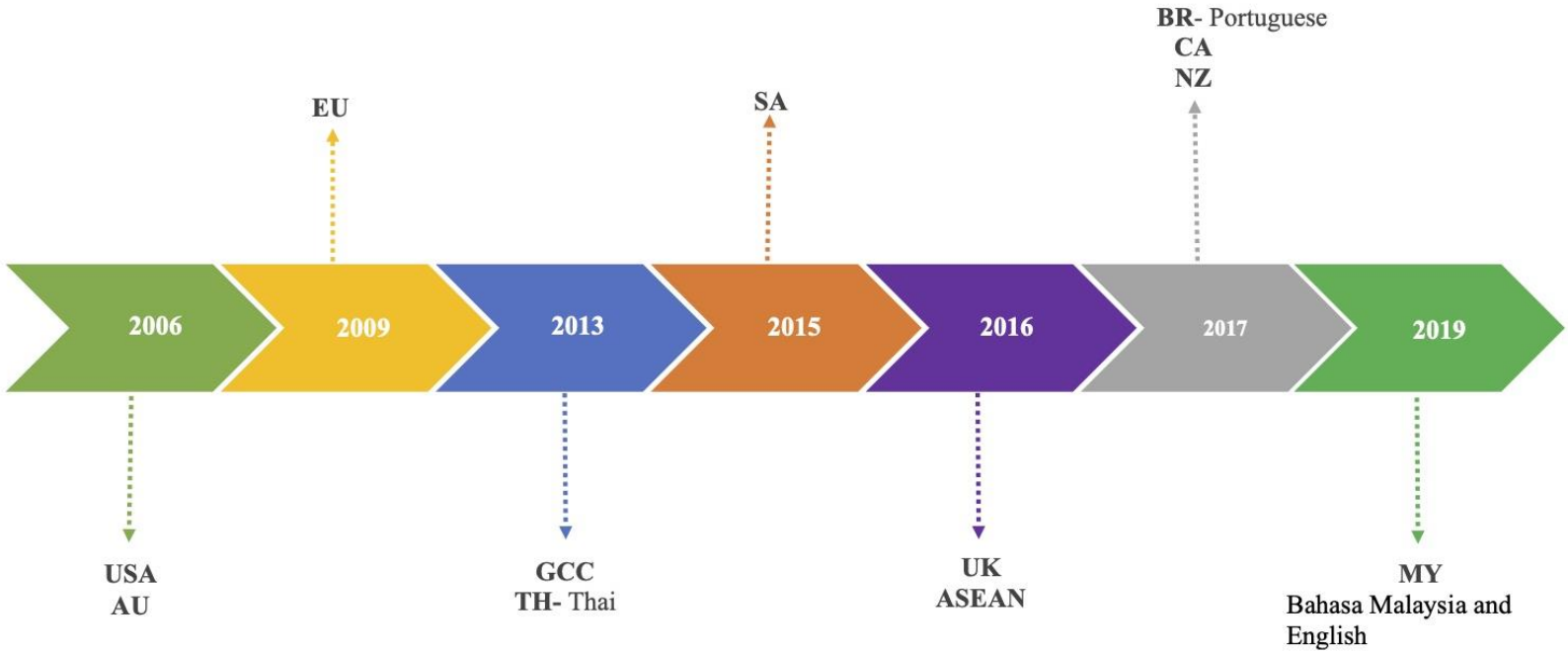

Fig.4.2 Timeline for latest editions and available Languages of PIL guidelines

4.2.2. Regulations of PILs in different regions

As a consideration for comparison of PILs regulations, table 4.7 presents the findings of comparisons including languages used for PILs and DRA websites. The languages used for PILs were varied depending on official languages of their countries or groups of countries. The manufactures were enforced by legislations to provide PILs of all drug classes in 41.7% of all guidelines: namely Canada, Malaysia, South Africa, UK and EU (39, 87) (13, 16, 90). Prescription medicines were needed to include leaflets for patients in almost all countries except Thailand in which PILs were provided for medicines which could be administered by consumers without prescription.

In this study, the availability of PILs were also investigated which were mostly attached in the carton box of drugs. The electronic format of PILs could be easily browsed and assessed by consumers onto 50% of 12 DRA websites whereas manufacturers provided only paper formats in other countries.

Table.4.7 Regulations of PILs across countries

Countries/ Groups of Countries	Drug Regulatory Authorities/ Websites	Name of Document/ Language	Classification of Drugs	Drug Required PILs	Channel of Distribution
AU	Therapeutic Goods Administration/ https://www.tga.gov.au/	Consumer Medicine Information/ English	1. Prescription Medicine 2. Over the Counter Medicine	√ √*	Package Website
BR	Brazilian Sanitary Surveillance Agency/ http://portal.anvisa.gov.br/english	Medicine Package Leaflet/ Not mentioned	1. Prescription Drug 2. Over the Counter Drug	√ √	Package
CA	Health Canada/ https://www.canada.ca/en/health-canada.html	Patient Medication Information leaflet/ Not mentioned	1. Prescription Drug 2. Over the Counter Drug	√ √	Package
MY	National Pharmaceutical Regulatory Division/ https://www.npra.gov.my/index.php/en/	Consumer Medication Information Leaflet (RiMUP)/ both English and Bahasa Malaysia	1. Prescription Medicine 2. Over the Counter Medicine	√ √	Package Website
NZ	New Zealand Medicines and Medical Devices Safety Authority/ https://www.medsafe.govt.nz/	Consumer Medicine Information/ English	1. Controlled Drug 2. Prescription Drug 3. Restricted Drug 4. Pharmacy only Drug 5. General Sale Drug	√ √ √ X X	Package Website

Table.4.7 Regulations of PILs across countries (continued)

Countries/ Groups of Countries	Drug Regulatory Authorities/ Websites	Name of Document	Classification of Drugs	Drug Required PILs	Channel of Distribution
SA	Medicine Control Council/ http://www.sanctr.gov.za/YourRights/TheMedicinesControlCouncil/tabid/176/Default.aspx	Patient Information Leaflet/ English and in at least one other official language	1. Prescription Medicine 2. Unscheduled Medicine 3. Over the counter Medicine	√ √ √	Package
TH	Food and Drug Administration/ http://www.fda.moph.go.th/sites/fda_en/Pages/Main.aspx	Patient Information Leaflet/ Thai	1. Controlled Substance 2. Dangerous Drug 3. Non-controlled and non-dangerous Drug 4. General Sale List Drug	X X √ √	Website Package
UK	Medicines and Healthcare products Regulatory Agency/ https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency	Package Leaflet/ English	1. Prescription medicine 2. Pharmacy medicine 3. General Sale List Medicine	√ √ √	Package Website
USA	Food and Drug Administration/ https://www.fda.gov/	Medication Guides/ English	1. Prescription Drug 2. Over the Counter Drug	√ X	Package Website
ASEAN	**	Patient Information Leaflet	**	**	**

Table 4.7 Regulations of PILs across countries (continued)

Countries/ Groups of Countries	Drug Regulatory Authorities/ Websites	Name of Document	Classification of Drugs	Drug Required PILs	Channel of Distribution
European Union	European Medicine Agency/ https://www.ema.europa.eu/en	Package Leaflet/ the official language or languages of the Member State(s)	1. Prescription Medicine 2. Over the Counter Medicine	√ √	Package
Gulf Cooperation Council	Executive Board of the Health Ministers' Council for GCC States/ http://agfund.org/partner/executive-board-of-the-health-ministers-council-for-gcc-states/	Patient Information Leaflet/ Arabic	**	**	**

*pharmacy only medicine

** Regulations are different among member countries

4.2.3. Comparison of designs and contents of PILs

A. Comparison of PIL designs

For the comparison, all data and contents were extracted and analyzed by content analysis. The published PILs guidelines from all countries or group of countries were not too much varied in terms paper designs used for PILs. The designs of PILs included type of paper to be used, number of columns, font and font size, line spacing, margin, length of sentences, pictures and tense usage.

All recommended number of columns were 3 which were only discussed in Australia, Malaysia and New Zealand (19, 87, 91). A serif font, Helvetica, Times New Roman and Tahoma were used, and font sizes for text were similar among all guidelines. The use of pictures and pictograms could be applied as an additional measure in case PILs make the message clearer to the patient in some guidelines. But Canadian DRA prohibited the use of pictograms not like other countries (39). The writing style content was recommended to use active voice to make patients more understandable. Although Australia TGA did not publish its own PILs guideline, they strongly recommended CMI creators to use it (19). But the DRAs of remaining countries developed their own guidelines.

Table 4.8 Comparison of PIL designs

Countries/ Group of Countries	#Column	Type of Paper	Font type and size	Line spacing	Margin	Use of Pictures	Length of Sentences	Tense usage
AU	3	A 4	Helvetica, Times	*	15mm for left, right, top and 20mm for bottom	*	not more than 20 words	active voice
CA	*	Portrait, A4	Sans Serif type fonts, 10 point for text and 9 points for table	*	7.5mm for all sides	should not be used	*	active voice
MY	3	*	Times New Roman, font size 24 and bold for title and 10 for text	single	*	*	*	*
SA	*	*	*	double	*	pictogram	not more than 20 words	*
TH	3	landscape A 4/ maximum 4 pages	Tahoma	*	*	*	*	*
EU	*	sufficiently thick	Times New Roman, 9	1.5 times	*	images, pictograms and other graphics	maximum 40 letters long	active style
GCC	*	*	Times New Roman, 9	1.5 times	*	*	*	active style

*Not discussed topics in their guidelines

Note: Brazilian guideline did not mention anything about PIL design, New Zealand included font size to be used (A serif font, font size 14 for Heading and 11 for normal text), the UK talking about using pictograms and the USA had font size to be used (10 points or larger

B. Comparison of PIL contents

For the purpose of comparison, contents were set up based on the sections in the EU QRD template and the others that did not included in it were added to the list. After the contents were added, all similar topics were extracted and created as a model PIL which contains 9 main headings as shown in Fig.4.3.

Regarding main heading of documents, the name of document such as " Patient Information Leaflet" or "Package leaflet: Information for the users" which appeared on the uppermost part of PIL was different among different regions. The additional information, the orders and wordings were found to be different. Among 12 guidelines, about 91.7% of them mentioned to include the contents "if you forget to take it" and "inactive ingredients". However, the other optional contents such as "Use in children and adolescents" and "Registration number" were included 25% and 33.3% of guidelines respectively.

Generally, almost all of PIL templates provided opening disclaimer for the patients to read the leaflets carefully before using their medications. However, guidelines of Australia, Malaysia and Thailand did not comprise of opening disclaimer while it was appeared in New Zealand guideline in which it was not in bold letters and not in separate section (19, 87, 88, 91). For the usage, it was written in lay languages as what drug class is this medication and it is used for which type of diseases to be easily understandable by the consumers. Although all the contents and orders were similar in all PIL guidelines, the USFDA recommended to state the

heading “What is the most important information I should know about (name of drug)?” after the title section (89). Moreover, the heading “serious side effects” appeared before any other contents of PIL in GCC guideline(92).

The name of document usually appears at the top of first page of each document and the brand name and generic name appears immediately below the words “PIL” or its synonyms in all PIL guidelines. Only 25% of guidelines mentioned the requirements to provide “phonetic pronunciation” on top of each PIL. In Australian and Malaysian guidelines, it was recommended to add pronunciation both for brand and generic names to make sure people can pronounce the name of medicine closely enough so that health care providers can understand what medicine patients are talking about (19, 87). But in USA, it was recommended that to add phonetic spelling for the brand name which is used throughout the Medication Guide (89).

“Dosage form” and “Strength” were mentioned in PILs of 75% of all guidelines. All the available strengths and dosage forms for each brand name were described not in title section but under the ingredient section of Australian guidelines while ACTD guideline and the US electronic code of federal regulations (e-CFR) part 208 did not mention about it (14, 19, 89). Malaysian guidance also allowed to use the same leaflet for different strengths, but it must be the same product name (87).

The ‘Warnings’ section composed of information about ‘contraindications’ and ‘interaction with other medicines’ in all PILs guidelines. But, the optional

contents such as care should be taken while ‘Pregnancy and breast feeding’ and ‘Driving and using machine’ only appeared in 58.3% and 50% of guidelines respectively while “Important information about some ingredients” was found in half of all guidelines. The US medication guide also included a statement about “geriatric risks” in under the heading of “What should I avoid while taking it?” (89).

Under the section of ‘Dosage and Administration’, all guidelines mentioned information about the ways to take medicines, usual dose and overdose. However, the additional information of when to take medicines was only in the 33.3% of PILs guidelines. The side effects of medicines were always described and sometimes divided into groups according to the strength or frequency. In Australia guideline, it was suggested that side effects were grouped by instructions about the kinds of action consumers need to take so that they would know exactly what to do. But in Canada, side effects were grouped by frequency and GCC guideline described that this section should include serious and major side effects as consistent with the black box warning in the SPC if applicable (39, 92).

The ways and contacts to report side effects for users were provided in half of all guidelines. Malaysia guideline also described that PILs must include compulsory statement: “You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03- 78835550 or visiting the website portal.bpfk.gov.my (Consumers Reporting)” at the end of side effects section event it is not in separate heading (87). In USA

regulation, the statement “Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.” Concerning about side effects reporting channels (87).

All the PIL guidelines suggested the consumers how to store medicines after using them. Most guidelines (66.7%) gave the instructions for consumers regarding with the information about how to dispose the medicines to reduce the environment from unwanted pollution. The appearance, ingredients, manufacturer or sponsor of each medicines, date of preparation of PILs were under the section of ‘Other Information’. In this section only ‘Manufacturer and Sponsor’ and ‘Date of Preparation of PILs’ were described in PILs of all guidelines. Sometimes manufacturer and CMI creator (Sponsor) were not the same and thus it described as “Manufacturer and Sponsor’ in the contents. The names and strengths of active and inactive ingredients were involved in almost all guidelines. Thailand PILs did not have contents for active and inactive ingredients and only active ingredient was described in the US PILs (88, 89).

Name of Document (PIL or its Synonyms)

Drug 'X'

(Active Ingredient)

What 'X' is used for?

Warnings

- Contraindications
- Interactions with other medicines
- Interactions with foods

How to take it?

- Usual Dose
- Overdose
- If you forget to take it

Possible Side Effects

- Side effects

How to store 'X'?

- Storage

More Information

- Manufacturer/ Sponsor
- Date of Preparation or Revision Date

Fig 4.3 Common and Similar Contents in PILs of all 12 guidelines

Table 4.9 Different contents in PILs guidelines across different regions

Contents		Countries/ Groups of Countries											n (%) of guideline describing each content
		AU	BR	CA	MY	NZ	SA	TH	UK	USA	ASEAN	EU	GCC	
Headings	Sub-headings													
Title Section	Phonetic Pronunciation	Brand, Generic	No	No	Brand, Generic	No	No	No	No	Brand only	No	No	No	3 (25)
	Dosage form	No*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	9 (75)
	Strength	No*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	9 (75)
What is in this leaflet?		Yes	No	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7 (58.3)
Warnings and Precautions	Pregnancy and Breast feeding	No	Yes	No	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	7 (58.3)
	Driving and Using Machine	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	6 (50)
	Important information about some ingredients	No	Yes	No	No	Yes	Yes	No	Yes	No	No	Yes	Yes	6 (50)
How to take it?	When to take it	Yes	Yes	No	Yes	Yes	No	No	No	No	No	No	No	4 (33.3)
	Use in children and Adolescents	No	No	No	No	No	No	No	Yes	Yes	No	Yes	No	3 (25)
	Duration of treatment	Yes	Yes	No	Yes	Yes	No	No	Yes	No	No	Yes	Yes	7 (58.3)
	If you forget to take it	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	11 (91.7)

Table 4.9 Different contents in PILs guidelines across different regions (continued)

Contents		Countries/ Groups of Countries												n (%) of guideline describing each content
		AU	BR	CA	MY	NZ	SA	TH	UK	USA	ASEAN	EU	GCC	
After using it	Disposal	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	8 (66.7)
Headings	Sub-headings													
Possible side effects	Reporting of side effects	No	No	Yes	Yes	No	No	No	Yes	Yes	No	Yes	Yes	6 (50)
Other information	Physical description	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9 (75)
	Inactive Ingredients	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	11 (91.7)
	Registration Number	Yes	Yes	No	Yes	No	Yes	No	No	No	No	No	No	4 (33.3)

*Dosage form and Strength were described under "**Other information**" section

4.2.4. Comparison of user testing

In the process of PILs development, some guidelines recommended to test PILs before submitting to DRAs. This type of testing has been called as user testing, diagnostic testing or consultation with target patient groups. According to EU guideline, user testing is intended to test the readability of a specimen with a group of selected test subjects and aims to identify whether or not the information as presented, conveys the correct messages to those who read it. Among 12 guidelines, only 5 countries, Australia, Canada, Thailand, UK and the EU, were found to have guidance for user testing of PIL development.

The results indicated that Canada used both readability and user testing in PIL development although other guidelines used only user testing. EU guideline allowed to use other methods if the outcome measures showed proved that patients can locate important information within the leaflet, understand it and enable the users to act appropriately (16). The requirements such as number of participants and success criteria used were found to be different among countries as shown in Table 4.10.

A. Requirements

For the requirements, only Thailand guideline discussed about inclusion criteria for participant's education level which has to be at least Grade 9. Moreover, all guidelines did not restrict for age or educational background for the characteristics

of participants. Time taken for the test range from 30-45 minutes and open-ended questionnaires which included 12-15 items was used in all guidelines. The numbers of participants needed were 10-11 in all guidelines although Canada had no explicit for this requirement. Pilot-testing was recommended to perform in Thailand, UK and EU guidelines (13, 16, 88). Canada did not discuss about the number of rounds to be tested, but Australia suggested to test the CMI until it performs at the optimum level (19, 39).

B. Success criteria

The acceptable success criterion for Thailand was 81% of participants had to find and answer the questionnaires which mean 64% was success criteria for 2 consecutive rounds. But Australia's passing criteria was that 81% were able to use CMI appropriately whereas EU and UK accepted that 80% of participants can find the information and answer the questions (13, 16, 19). There were not any success criteria in Canada guideline (39).

Table 4.10 Comparison of user testing in PILs guidelines

Requirements	Countries/ Groups of Countries				
	AU	CA	TH	UK	EU
Education of Participants	Not discussed	Not discussed	Grade 9	Not discussed	Not discussed
Time Taken	30-35 minutes	30-35 minutes	30-35 minutes	45 minutes	45 minutes
#Questions	15 items	15items	12-15 items	12-15 items	12-15 items
Types of Questions	Open-ended	Open-ended	Open-ended	Open-ended	Open-ended
Pilot-testing	Not discussed	Not discussed	2-6 participants	3-6 participants	3-6 participants
#Participants	10	Not discussed	10-11	10	10
Success criteria	90% of able to find and at least 90% of them able to act appropriately on the information	Not discussed	90% find the answer and 90% of them answer correctly by their own word	90% find the answer and 90% of them answer correctly by their own word	90% find the answer and 90% of them answer correctly by their own word
	81% able to use CMI appropriately	Not discussed	81% of them find and answer	16 out of 20 them find and answer	16 out of 20 them find and answer
#Rounds	Repeated until the CMI performs at optimum level	Not discussed	2 consecutive rounds	2 consecutive rounds	2 consecutive rounds

CHAPTER V- DISCUSSION AND CONCLUSION

The first objective of this study aimed to assess current situation regarding provision of drug information to Myanmar people at community pharmacies in Yangon region. This part evaluated drug information attached with the drug products and investigated verbal and written drug information provided by the drug dispensers in community pharmacies for the first objective. Content analysis was used to analyze drug information provided along with 30 drug samples of 3 drug categories. Before performing the survey in Yangon, the request letter was sent to the Yangon Food and Drug Supervisory Committee. The chairperson of that committee issued the approved letter and also sent the informed letter to the 6 selected townships level Food and Drug Supervisory Committee about the process of survey. After getting approval, the simulated patient stratified single stage cluster sampling was used to recruit appropriate samples and survey at all community pharmacies in the selected townships of Yangon region.

To fulfil the second objective this study, targeted literature review was performed. This was the first study which explored PIL using countries and reviewed and compared PILs guidelines. Literature search on google was performed and all the DRA websites were also explored to find the PILs using countries around the world. The PILs guidelines of all the resulted countries were reviewed and compared by content analysis.

5.1. Current situation of drug product provision for Myanmar consumers

The first part of this study evaluated the availability of drug product information for Myanmar consumers to know how much they receive drug information. The situation analysis was conducted by using content analysis and simulated patient survey. The drug information assessed in the present study were information provided along with drug products and information provided by the dispensers of community pharmacies. Additionally, the other influencing factors such as characteristics of carton boxes, leaflets and pharmacies' information such as the presence of pharmacist in the pharmacy were also investigated.

As can be seen from both content analysis and simulated patient study, Myanmar consumers might not seem to get understandable drug information and the available information were also not enough. According to the Regulations on National Drug Law 1993, all drugs registered in Myanmar must be labelled, all prescriptions drugs must include package leaflets and must be provided in Myanmar or English or both languages (24). Based on the evaluation of 30 drug products of all drug categories in Myanmar, both carton boxes and leaflets of drugs were mostly available in English language although font size and types used seemed to be readable. Regarding simulated patient survey of this study, patients usually do not get enough medication information since the majority of dispensers did not provide drug information especially in written form. In addition, the results indicated that the

mean scores of overall drug information was 4.13±2.028 for all dispensers (maximum score is 18) and thus some dispensers cannot provide drug information correctly.

To our knowledge, the content analysis of drug information attached with drug products is the first study in Myanmar. The evaluation of 30 drug products showed that the leaflet of only one drug (3.3%) was available in both Myanmar and English languages which might be understandable for lay persons. Most Myanmar people might not read and understand English language as they have very low proficiency score for English Proficiency Index (EF EPI) which was 46 in 2019 (93). Besides, about contents in 86.7% of leaflets were intended for healthcare professionals use although contents described on all the carton boxes were understandable for consumers. The information provided on the carton boxes were not complete for medication usage and patients might not get these carton boxes unless they bought all drugs in the carton boxes.

During simulated patients approach at community pharmacies, most dispensers did not intend to provide drug information if they were not asked for. Majority were not pharmacists and in the same way, the findings in perception and practice of drug sellers on antibiotic sales without prescription also showed that only 4.9% of dispensers were trained pharmacists who could give the right answers for all statements about the role of antibiotics. Although patients have to rely on information provided by the dispensers, only dosage information was provided

verbally by most of the dispensers. Assessment of the drug information services also showed low range.

In this study, the mean scores for overall drug information service scores were low and there was no significant difference between pharmacists and non-pharmacists. The similar result was found in a Turkish study of dispensing practice in community pharmacies in which dispensers; qualification did not influence dispensing scores (83). On the other hand, a recent study of Zawahir et al. pharmacists had significant higher overall mean knowledge scores about antibiotic dispensing in Sri Lanka (94). Since the ratio of healthcare professional and population is low in Myanmar (78), most of the non-pharmacist dispensers have usually trained in 3-month pharmacy training school and the rests are the relatives of pharmacy shops owners. Therefore, it can be assumed that better dispensing habit might be occurred if they have long term experience of dispensing practices.

On the other hand, the proxy drug used in secret shopping is familiar and simple to use for consumers. The pitfall of this scenario seems to impact the drug information provision behavior of dispensers since they might think that most patients can take it easily. The subgroup analysis for pharmacists and non-pharmacists resulted in no significant difference in mean scores of overall drug information services. However, there might be an increase in frequency, or mean scores of information services provided by pharmacists if more complex drug or different scenarios is used.

Additionally, the workload was not an influencing factor for drug information services in this research. The dispensers who had to handle a few consumers (0-3) or crowded conditions (> 3) were found to have similar drug information service scores in general. The study of Caamano et al. suggested that the pharmacies with excessive workload function might reduce patient-dispenser interaction time and control over dispensing services might be lessen (63). Their suggestion did not also comply with the present study of pharmacies in Yangon region.

Because of the low literacy rate and shortage in health care professionals, Myanmar consumers have to rely on the information provided in the drug products and by the dispensers, there should be implementation of patient information leaflets. The ASEAN countries including Thailand and Malaysia have their own guidelines and enforced to provide leaflets for consumers in local languages. Singapore Health Science Authority (HSA) also provides electronic consumer medicine information on their official websites although they do not have guidelines (45).

The results from this study stated that Myanmar consumers do not get enough drug information from both from the products they bought and from the dispensers of community pharmacies. Starting April 2019, Consumer Protection Law was enacted and most of the pharmaceutical companies had ben implementing the use of Myanmar language to describe summary of medication usages on the carton boxes of OTC products (25). But OTC drug leaflets and both carton boxes and

leaflets of other drug categories were not available in Myanmar languages. Moreover, the dispensers could not also provide drug information regarding history taking, verbal and written drug information. Therefore, the findings suggested that Myanmar consumers might need education materials which are written in native language and lay terms for their safe and effective use of medications.

5.2. Review and comparison of international PIL guidelines

For the purpose of second objective of this study, targeted review was conducted to compare the regulations, designs, contents and user testing of PILs from different DRAs around the world. It was found that there were 12 PILs development guidelines and data were extracted from DRA websites of 9 countries and 3 groups of countries. The terms used to call PILs and updated year of latest version for PILs guidelines were varied. The essential contents and designs were similar among regulatory agencies and the difference in optional contents might depend on the time when PILs guidelines were last updated.

According to the list of countries from World Bank data, only about 21% of countries around the world were found to use PILs development guideline and their DRAs enforced pharmaceutical companies to provide PILs while applying for marketing authorization. A few countries (about 11%) were interested to implement the use of PILs and conducting the researches related to development or user

testing of PILs. Among high-income countries that use PILs guideline, DRAs of all countries need to provide PILs for controlled and prescription only medicines.

But for upper- middle income countries, prescription only medicines do not require PILs in Malaysia and controlled substance and dangerous drug do not need to provide PILs in Thailand. While looking through the channel of distribution for PILs, most of the high-income countries except Canada provide PILs on their DRA websites in addition to in the pack of medicines. On the other hand, consumers can access PILs only on websites of Thailand and Malaysia among upper middle- income countries having own PILs development guidelines.

The main heading (title section) seems to be similar in all guidelines except phonetic pronunciation, dosage form and strength. Although the provision of phonetic pronunciation is probably intended to aid consumer to call medicine correctly, it may not necessary. In Australia and US guidelines, dosage form and strength did not describe at the very beginning of PILs. By looking this, they may probably want to use only one PIL for all dosage forms and strengths for one drug.

The contents and orders of PILs from Australia, New Zealand and Malaysia are identical except Malaysia has information for consumers to report side effects to the DRAs while UK and EU have the same PIL format called QRD (Quality Review of Documents) template (95). The difference in composition of information for disposal and reporting side effects of medicines may depend on each country's regulation system. The countries that have information about disposal of medicines in PILs

contents are high income countries except Canada. ‘Reporting of side effects’ section did not include in contents of all PILs guidelines. This may be the timeline of updated version of PIL guidelines, implementation time of Risk Management Plan (RMP) and reporting of side effects. For instance, the implementation of RMP in Australia was in 2012 (96), but the updated version of PIL guideline was in 2006. And thus, Australia guideline did not mention about how to report side effects by the consumers. In the same way, EU and UK had the information for reporting side effects because their guidelines were updated after regulations of RMP in 2005 (97).

5.3. Limitations of research and further research recommendation

In the evaluation of drug product information provision, all drug categories for most dispensing drugs in pharmacies were included and it represented evaluation of drug product information registered in Myanmar. But the proxy drug used for simulated patient visit was Mefenamic Acid which represented only one drug category, POM. As four simulated patients were included in the survey, inequality in collected data that might cause bias and they may also forget detailed information provided by the dispensers. To generalize all community pharmacies, survey with larger sample sizes was recommended with the updated lists of registered pharmacies.

Regarding targeted literature review, this study was the first study that compared development guidelines and regulations of PILs among different DRAs. The

present targeted review was performed by screening of two independent reviewers for the relevance. Other than the literature search on Google, DRA websites of all countries were looking through by two reviewers to include almost all countries that had been using PILs guidelines. But this review also has some limitations because it contained only published articles and may not be included countries that were not published their articles or using PILs guidelines. Moreover, some countries which were using other words for PILs were not found since we used only six synonyms of PILs for literature search. Countries with rigorous DRAs would be more likely to publish researches in English and all PILs using countries might not be included as we used only English language. Therefore, it is suggested that future research perform survey with key informants all over the world by asking them to provide information about PILs guidelines or researches from their counties and other source of information related to PILs.

5.4. Conclusion

The drug product information provided in most of the drugs complied with the regulations in Myanmar, but the information was in mostly English and only intended for health care professional uses. The information provided by the dispensers were not also sufficient for consumers. Therefore, the implementation of regulations for patient information leaflets seems to be effective for the safe and effective use of drugs by the patients in Myanmar.

The targeted review sought to extract and compare regulations and guidelines of PILs regarding contents and designs in different DRAs of different countries. Australia and USA have partially outdated information with regards to contents such as 'Reporting of Side Effects' although they are high-income countries, and their guidelines need a complete update. Only 6 out of 12 countries or groups have provision of PILs on their websites, although the use of smart phones and internet usage is very common. Practical implementations are required for the use of PILs and the establishment of up-to-date guideline to create PILs with appropriate standards and appropriate form. The findings of this review also emphasize on strength and weakness of different PILs guidelines. PILs should be as direct and simple as possible and it is essential that information provided is clearly understandable for patients to take action effectively.

It is clear that all the guidelines from this study could have the common leaflet contents which are essential for patient medication uses. Despite the US was the first country that started to use leaflets for patients (70), it seemed that most of the guidelines had used the EU guideline as a reference. The EU guideline is likely to be most suitable guideline to be used for PIL development although their guideline was last updated in 2009 (16).

Overall, the labelling requirements in terms of language use should be well regulated as a first step. Even the implementation of PILs guideline could not established for our own, the contents for PILs were mentioned in ACTD guideline and

it can be used as a reference. Finally, the results from targeted review of this study will become a support for Myanmar FDA if the use of PIL needed to be well regulated and tested with Myanmar consumers.

APPENDICES

Appendix I- Population Density of Yangon Region and Stratification for Sampling

No.	Township	Density (Population per Area km^2)	Strata
1	Pabedan	53,652	1
2	Pazuntaung	45,089	2
3	Kyauktada	42,566	2
4	Sangyoung	41,572	2
5	Latha	41,543	2
6	Lanmadaw	35,972	3
7	Tamway	33,136	3
8	Mingala Taungnyunt	26,763	4
9	Kyimyindine	25,015	4
10	Dawbon	24,114	4
11	South Okkalapa	19,581	5
12	Ahlon	16,394	5
13	Thakayta	16,390	5
14	Thingangyun	15,953	5
15	Hline	15,734	5
16	Botahtaung	15,711	5
17	Yankin	14,821	5
18	Kamayut	13,040	5
19	North Okkalapa	11,991	5
20	Bahan	11,404	5
21	Insein	10,230	5
22	Dagon Myothit (South)	9,906	6
23	Dagon Myothit(North)	8,432	6
24	Hlinethaya	8,229	6
25	Mayangon	7,329	6

No.	Township	Density (Population per Area km2)	Strata
27	Dagon	5,217	6
28	Seikkyi/ Khanaungto	2,808	6
29	Mingaladon	2585	6
30	Seikkan	2,406	6
31	Dagon Myothit(Seikkan)	2,179	6
32	Dagon Myothit (East)	1,207	6
33	Dala	755	6
34	Thanlyin	745	6
35	Hmawby	519	6
36	Twantay	314	6
37	Khayan	248	6
38	Htantabin	243	6
39	Thongwa	219	6
40	Kyauktan	208	6
41	Kawhmu	193	6
42	Kungyangon	187	6
43	Hlegu	178	6
44	Taikkyi	157	6
45	Cocogyun	42	6

Appendix II- Search Strategy

Google

1# - Search (Patient Information Leaflet) AND Name of each country from World Bank list

2# - Search (Patient Package Insert) AND Name of each country from World Bank list

3# - Search (Consumer Medicine Information) AND Name of each country from World Bank list

4# - Search (Package Leaflet) AND Name of each country from World Bank list

5# - Search (Drug Guide for Patient) AND Name of each country from World Bank list

6# - Search (Package Insert) AND Name of each country from World Bank list

REFERENCES

1. World Health Organization. WHO policy perspectives on medicines- Promoting rational use of medicines: core components. 2002. http://archives.who.int/tbs/rational/h3011e.pdf. Assessed 12 May 2019

2. Saqib A, Atif M, Ikram R, Riaz F, Abubakar M, Scahill S. Factors affecting patients' knowledge about dispensed medicines: A qualitative study of healthcare professionals and patients in Pakistan. PLOS ONE. 2018;13(6):e0197482.

3. Laws M, Lee Y, Taubin T, Rogers W, Wilson I. Factors associated with patient recall of key information in ambulatory specialty care visits: Results of an innovative methodology. PLOS ONE. 2018;13:e0191940.

4. Chambers CT, Reid GJ, McGrath PJ, Finley GA. Self-administration of over-the-counter medication for pain among adolescents. Archives of Pediatrics & Adolescent Medicine. 1997;151(5):449-55.

5. Bryden P, Fletcher P. Knowledge of the risks and benefits associated with oral contraception in a university-aged sample of users and non-users. Contraception. 2001;63:223-7.

6. Peremans L, Hermann I, Avonts D, Royen P, Denekens J. Contraceptive knowledge and expectations by adolescents: An explanation by focus groups. Patient education and counseling. 2000;40:133-41.

7. Davis TC, Wolf MS, Bass PF, 3rd, Middlebrooks M, Kennen E, Baker DW, et al. Low literacy impairs comprehension of prescription drug warning labels. Journal of general internal medicine. 2006;21(8):847-51.

8. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The common technical documents (CTD). https://www.ich.org/page/ctd. Assessed 12 May 2019

9. European Medicine Agency. Product information requirements. https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information-requirements. Assessed 12 May 2019

10. Raynor DKT, Svarstad B, Knapp P, Aslani P, Rogers MB, Koo M, et al. Consumer medication information in the United States, Europe, and Australia: A comparative evaluation. Journal of the American Pharmacists Association. 2007;47(6):717-26a.

11. Herber O, Gies V, Schwappach D, Thürmann P, Wilm S. Patient information leaflets: Informing or frightening? A focus group study exploring patients' emotional reactions and subsequent behavior towards package leaflets of commonly prescribed medications in family practices. BMC family practice. 2014;15:163.

12. Therapeutic Goods Administration. Therapeutic goods rrder no. 69—General requirements for labels for medicines.2017. https://www.legislation.gov.au/Details/F2017L00865. Assessed 12 May 2019

13. Medicines and Healthcare products Regulatory Agency (MHRA). Best practice in the labelling and packaging of medicines. 2014.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/474366/Best_practice_guidance_labelling_and_packaging_of_medicines.pdf. Assessed 12 May 2019

14. The Association of Southeast Asian Nations (ASEAN). The ASEAN common technical dossier (ACTD) for the registration of pharmaceuticals for human use. 2016. https://asean.org/storage/2017/03/68.-December-2016-ACTD.pdf. Assessed 12 May 2019

15. Patil M, Kandhare A, Bhise S, Bhale S. Evaluation of patient information leaflets on basis of consumer psychology and opinion. International Journal of Pharmacy and Pharmaceutical Science Research. 2011;1:87-92.

16. European Commission. Guideline on the readability of the labelling and package leaflet of medicinal products for human use. 2009. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/2016_12_packaging_guidelines_revision_14_4.pdf. Assessed 12 May 2019

17. Raynor DK, Knapp P, Silcock J, Parkinson B, Feeney K. "User-testing" as a method for testing the fitness-for-purpose of written medicine information. Patient Education and Counseling. 2011;83(3):404-10.

18. Raynor DK. User testing in developing patient medication information in Europe. Research in Social and Administrative Pharmacy. 2013 Sep 1;9(5):640-5.

19. Sless D, Wiseman R. Writing about medicines for people: usability guidelines for consumer product information. Department of Health & Family Services; 2006.

20. Achin J, Venkatesh MP, Pramod K. ACTD: Bridge between regulatory requirements of developed and developing countries. International Journal of Drug Regulatory Affairs. 2013 Dec 1;1(4):1-1.

21. World Health Organization. The Republic of the Union of Myanmar Health system review: WHO Regional Office for the Western Pacific. 2014.

22. Pwint KH, Win NN, Wun M, Aye MM, Aung T, Aung SS, et al. Perception and practice of drug sellers in selected townships in Yangon region on antibiotic sales without prescription. 44th Myanmar Health Research Congress2016. p. 39-40.

23. Win NN, Pwint KH, Wun M, Aye MM, Aye PP, Myint KK, et al. Perception and practice of private pharmacies in Nyaung Lay Pin Township on antibiotic sales without prescription. 44th Myanmar Health Research Congress2016. p. 40-1.

24. Ministry of Health and Sports. Myanmar. Regulations on national drug law. 1993. http://www.fdamyanmar.gov.mm/wp-content/uploads/2018/01/Regulations-on-National-Drug-Law-min.pdf. Assessed 12 May 2019

25. Central Committee of Consumer Protection. Myanmar. Consumer protection law. 2019. http://www.myanmar-law-library.org/law-library/laws-and-regulations/laws/myanmar-laws-1988-until-now/national-league-for-democracy-2016/myanmar-laws-2019/pyidaungsu-hluttaw-no-9-2019-consumer-protection-law-burmese.html. Assessed 12 May 2019

26. Shrank W, Avorn J, Rolon C, Shekelle P. Medication safety: Effect of content and format of prescription drug labels on readability, understanding, and medication use: A systematic review. Annals of Pharmacotherapy. 2007 May;41(5):783-801.

27. Bailey SC, Navaratnam P, Black H, Russell AL, Wolf MS. Advancing best practices for prescription drug labeling. Annals of Pharmacotherapy. 2015 Nov;49(11):1222-36.

28. Wali H, Hudani Z, Wali S, Mercer K, Grindrod K. A systematic review of interventions to improve medication information for low health literate populations. Research in Social and Administrative Pharmacy. 2016 Nov 1;12(6):830-64.

29. Garfield S, Barber N, Walley P, Willson A, Eliasson L. Quality of medication use in primary care-mapping the problem, working to a solution: a systematic review of the literature. BMC medicine. 2009 Dec;7(1):50.

30. Notenboom K, Leufkens HG, Vromans H, Bouvy ML. Learning from patients: Identifying design features of medicines that cause medication use problems. International Journal of Pharmaceutics. 2017 Jan 30;517(1-2):128-34.

31. Notenboom K, Beers E, van Riet-Nales DA, Egberts TC, Leufkens HG, Jansen PA, Bouvy ML. Practical problems with medication use that older people experience: a qualitative study. Journal of the American Geriatrics Society. 2014 Dec;62(12):2339-44.

32. Management Sciences for Health and World Health Organization. Drug and therapeutics committee training course. Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health. 2007.

33. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, et al. Incidence of Adverse Drug Events and Potential Adverse Drug Events: Implications for Prevention. JAMA. 1995;274(1):29-34.

34. European Medicines Agency (EMA). Guideline on good pharmacovigilance practices (GVP). Module V–Risk management systems. 2017. p. 36.

35. Field TS, Mazor KM, Briesacher B, DeBellis KR, Gurwitz JH. Adverse drug events resulting from patient errors in older adults. Journal of the American Geriatrics Society. 2007 Feb;55(2):271-6.

36. Mira JJ, Nebot C, Lorenzo S, Pérez-Jover V. Patient report on information given, consultation time and safety in primary care. Quality and Safety in Health Care. 2010 Oct 1;19(5):e33-.

37. Mira JJ, Orozco-Beltrán D, Pérez-Jover V, Martínez-Jimeno L, Gil-Guillén VF, Carratala-Munuera C, Sánchez-Molla M, Pertusa-Martínez S, Asencio-Aznar A. Physician patient communication failure facilitates medication errors in older polymedicated patients with multiple comorbidities. Family practice. 2013 Feb 1;30(1):56-63.

38. Emmerton LM, Mampallil L, Kairuz T, McKauge LM, Bush RA. Exploring health literacy competencies in community pharmacy. Health Expectations. 2012 Mar;15(1):12-22.

39. Health Canada. Health Products and Food Branch. Guidance for industry: Product monograph. 2016. https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-

mps/alt_formats/pdf/prodpharma/applic-demande/guide-ld/monograph/pm-guid-ld-mp-eng.pdf. Assessed 12 May 2019

40. Bauschke R. Regulatory agencies, pharmaceutical information and the internet: a European perspective. Health Policy. 2012 Jan 1;104(1):12-8.

41. The United States Food and Drug Administration. Human drugs. http://www.fda.gov/industry/regulated-products/human-drugs. Assessed 12 May 2019

42. The United States Food and Drug Administration. Learn about your medicines. http://www.fda.gov/patients/learn-about-your-medicines. Assessed 12 May 2019

43. Therapeutic Goods Administration. Medicine information and labelling. https://www.tga.gov.au/book-page/13-medicine-information-and-labelling. Assessed 12 May 2019

44. The Association of Southeast Asian Nations (ASEAN). The ASEAN common technical dossier (ACTD) for the registration of pharmaceuticals for human use, Part I : Administrative data and product information. 2002. https://www.nihcollaboratory.org/sites/CbyC/regional/Document%20Library/Forms/AllItems.aspx. Assessed 12 May 2019

45. Health Science Authority. Guidance on therapeutic product registration in Singapore. Appendix 7, Points to consider for Singapore labelling. 2016. https://www.hsa.gov.sg/docs/default-source/hprg/therapeutic-products/guidance-documents/appendix-7_points-to-consider-for-singapore-labelling.pdf. Assessed 12 May 2019

46. Berman A. Reducing medication errors through naming, labeling, and packaging. Journal of medical systems. 2004 Feb 1;28(1):9-29.

47. Sustersic M, Tissot M, Tyrant J, Gauchet A, Foote A, Vermorel C, Bosson JL. Impact of patient information leaflets on doctor–patient communication in the context of acute conditions: a prospective, controlled, before–after study in two French emergency departments. BMJ open. 2019 Feb 1;9(2):e024184.

48. Michel B, Hemery M, Rybarczyk-Vigouret MC, Wehrlé P, Beck M. Drug-dispensing problems community pharmacists face when patients are discharged from hospitals: a study about 537 prescriptions in Alsace. International Journal for Quality in Health Care. 2016 Dec 1;28(6):779-84.

49. Mackridge AJ, Rodgers R, Lee D, Morecroft CW, Krska J. Cross‐sectional survey of patients' need for information and support with medicines after discharge from hospital. International Journal of Pharmacy Practice. 2018 Oct;26(5):433-41.

50. European Patients Forum. Informed patients can help prevent medication errors. https://www.eu-patient.eu/News/News-Archive/informed-patients-can-help-prevent-medication-errors/#:~:text=By%20being%20aware%20of%20the,intercept%203%25%20of%20medication%20errors. Assessed 12 May 2019

51. Poornima D, Ramesh A. Assessment of patient information leaflets usefulness in selected chronic diseases-A south Indian based study. Indian Journal of Pharmacy Practice. 2014 Jan;7(1):23.

52. Mansoor L, Dowse R. Written medicines information for South African HIV/AIDS patients: Does it enhance understanding of co-trimoxazole therapy? Health education research. 2007;22:37-48.

53. Sustersic M, Gauchet A, Foote A, Bosson JL. How best to use and evaluate Patient Information Leaflets given during a consultation: a systematic review of literature reviews. Health Expectations. 2017 Aug;20(4):531-42.

54. Yin HS, Dreyer BP, van Schaick L, Foltin GL, Dinglas C, Mendelsohn AL. Randomized controlled trial of a pictogram-based intervention to reduce liquid medication dosing errors and improve adherence among caregivers of young children. Archives of pediatrics & adolescent medicine. 2008 Sep 1;162(9):814-22.

55. World Health Organization. How to investigate the use of medicines by consumers. World Health Organization; 2004.

56. Xu T, de Almeida Neto A, Moles R. A systematic review of simulated-patient methods used in community pharmacy to assessthe provision of non-prescription medicines. The International journal of pharmacy practice. 2012;20:307-19.

57. Björnsdóttir I, Granas A, Bradley A, Norris P. A systematic review of the use of simulated patient methodology in pharmacy practice research from 2006 to 2016. International Journal of Pharmacy Practice. 2019;28.

58.Murphy AL, Gardner DM. A simulated patient evaluation of pharmacist's performance in a men's mental health program. BMC research notes. 2018 Dec 1;11(1):765.

59. World Health Organization. Rational use of drugs. Report of a conference of experts, Nairobi. November 1985. Geneva: WHO 1997.

60. Toklu H. The pharmacy practice of community pharmacists in Turkey. Marmara Pharmaceutcal Journal. 2010;1:53-60.

61. Laing R. Role of dispensers in promoting rational drug use. 2009. http://archives.who.int/PRDUC2004/RDUCD/Session_Guides/role_of_dispensers_in_rational_d.htm.

62. Ansari M. Evaluation of community pharmacies regarding dispensing practices of antibiotics in two districts of central Nepal. PLOS ONE. 2017;12:e0183907.

63. Caamano-Isorna F, Tomé-Otero M, Takkouche B, Gestal Otero JJ. Influence of pharmacists' opinions on their dispensing medicines without requirement of a doctor's prescription. Gaceta sanitaria / SESPAS. 2005;19:9-14.

64. Lenjisa JL, Mosisa B, Woldu MA, Negassa ED. Analysis of dispensing practices at community pharmacy settings in Ambo Town, West Shewa, Ethiopia. Journal of Community Medicine & Health Education. 2005;05:329.

65. Kamuhabwa AR, Ignace AM. Dispensing practice of prescribed medicines in the private pharmacies in urban areas of Tanzania. Indian journal of pharmaceutical sciences. 2015 Sep;77(5):542.

66. Cohen MM, Dunn S, Cockerill R, Brown TE. Using a secret shopper to evaluate pharmacist provision of emergency contraception: satisfaction levels high, with

privacy a concern. Canadian Pharmacists Journal/Revue des Pharmaciens du Canada. 2004 Feb;137(1):28-33.

67. Collins J, Schneider C, Naughtin C, Wilson F, de Almeida Neto A, Moles R. Mystery shopping and coaching as a form of audit and feedback to improve community pharmacy management of non-prescription medicine requests: an intervention study. BMJ Open. 2017;7:e019462.

68. Alte D, Weitschies W, Ritter CA. Evaluation of consultation in community pharmacies with mystery shoppers. Annals of Pharmacotherapy. 2007 Jun;41(6):1023-30.

69. Young A, Tordoff J, Smith A. Regulatory agencies' recommendations for medicine information leaflets: Are they in line with research findings?. Research in Social and Administrative Pharmacy. 2018 Feb 1;14(2):196-202.

70. Raynor TDK. Consumer medicines information : an international perspective. The Chronic ill. 2003(7):4-7.

71. Yuan H-C, Raynor D, Aslani P. Comparison of International Regulations for Written Medicine Information (WMI) on Prescription Medicines. Therapeutic Innovation & Regulatory Science. 2018;53:216847901877694.

72. Tandon A, Murray CJ, Lauer JA, Evans DB. Measuring overall health system performance for 191 countries. Geneva: World Health Organization. 2000.

73. Kyaing NN, Sein T, Sein AA, Htike MT, Tun A, Shein NN. Smokeless tobacco use in Myanmar. Indian Journal of Cancer. 2012 Oct 1;49(4):347.

74. World Health Organization. Medicine in healthcare delivery Myanmar: Situational analysis. WHO Regional Office for South East Asia, New Delhi, India; 2014.

75. Latt N, Cho SM, Htun NMM, Saw Y, Myint M, Aoki F, et al. Healthcare in Myanmar. Nagoya Journal of Medical Science. 2016;78:123-34.

76. Data for the sustainable development goals Myanmar . 2016. http://uis.unesco.org/en/country/mm. Assessed 12 May 2019

77. Oo WM, Soe PP, Lwin KT. Status and determinants of health literacy: a study among adult population in selected areas of Myanmar. Int J Res Med Sci. 2015 Jul;2:318-22.

78. Saw Y, Than T, Thaung Y, Aung S, Shiao L, Win E, et al. Myanmar's human resources for health: Current situation and its challenges. Heliyon. 2019;5:e01390.

79. Myanmar Food and Drug Administration.National Drug Law. 1992. http://www.fdamyanmar.gov.mm/wp-content/uploads/2018/01/Drug-Regulation.pdf. Assessed 12 May 2019

80. International Pharmaceutical Federation. FIP Statement of Policy. Strategic development of medicines information for the benefit of patients and users of medicines2017.

81. Chauhan S. A Review on the Healthcare System & Pharmaceutical Market of Myanmar A report.2017.

82. Ghosh J, Pandey A, Soe Z. Myanmar pharma generic market - A brief abstract on how it was and presently how it is. Journal of Generic Medicines: The Business Journal for the Generic Medicines Sector. 2014;11:48-51.

83. Gokcekus L, Toklu H, Demirdamar R, Gumusel B. Dispensing practice in the community pharmacies in the Turkish Republic of Northern Cyprus. International journal of clinical pharmacy. 2012;34:312-24.

84. The United Nations Development Programme (UNDP) Myanmar. The State of Local Governance: Trends in Yangon. 2015. p. 112.

85. The World Bank. World bank country and lending groups 2019 [Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519.

86. Brazilian National Health Surveillance Agency, RESOLUÇÃO-RDC No 47, DE 8 DE SETEMBRO DE 1 2009 (*) . 2009. http://portal.anvisa.gov.br/documents/33836/2814380/RDC+47+09.pdf/c8e87008-a27d-435e-b137-f51e02e45858. Assessed 12 Jan 2019

87. National Pharmaceutical Regulatory Agency (NPRA). Garispanduan pelaksanaan risalah maklumat ubat untuk pengguna (RiMUP). 2019.

88. Thai Food and Drug Administration. Guideline for leaflet development. 2013. http://www.fda.moph.go.th/sites/drug/Shared%20Documents/Law04-Notification-ThFDA/FDA-20130703.pdf. Assessed 12 May 2019

89. Food and Drug Administration. Guidance: Useful written consumer medication information (CMI). Rockville, MD: US Food and Drug Administration. 2006.

90. South African Health Products Regulatory Authority, Guideline for patient information leaflet for human medicines categories A and D. 2019. https://sahivsoc.org/Files/2.14_guideline%20for%20patient%20information%20leaflet%20for%20hum an%20medicines%20(categories%20a%20and%20d)_jul19_v2.pdf. Assessed 12 Jan 2019

91. New Zealand Medicines and Medical Device Safety Authority. Guideline on the regulation of therapeutic products in New Zealand; Part 10. 2013. https://www.medsafe.govt.nz/regulatory/Guideline/GRTPNZ/Part10.pdf. Assessed 12 May 2019

92. Executive Board of the Health Ministers' Council for GCC States. The GCC guidance for presenting the SPC, PIL and labeling information. 2013. https://www.sfda.gov.sa/en/drug/drug_reg/Regulations/Guidance%20for%20SPC%20PIL%20SFDA%20version%202.0.pdf. Assessed 12 May 2019

93. EF English Proficiency Index – Myanmar [Internet]. 2019. https://www.ef.com/wwen/epi/regions/asia/myanmar/. Assessed 12 May 2019

94. Zawahir S, Lekamwasam S, Aslani P. A cross-sectional national survey of community pharmacy staff: Knowledge and antibiotic provision. PloS one. 2019 Apr 25;14(4):e0215484.

95. European Medicines Agency. QRD Human Product Information Templates; Centralised procedures – version 10. 2016. https://www.ema.europa.eu/en/human-

regulatory/marketing-authorisation/product-information/product-information-templates. Assessed 12 May 2019

96. Therapeutic Goods Administration. Risks management plan for medicines and biologicals: Australian requirements and Recommendations.2019. https://www.tga.gov.au/sites/default/files/risk-management-plans-medicines-and-biologicals.pdf. Assessed 12 May 2019

97. Bührlen B, Reiß T, Beckmann C, Gassner UM, Gleiter CH. Assessment of the European community system of pharmacovigilance. Fraunhofer-IRB-Verlag; 2006.

VITA

NAME	MS. ZAR NI WIN
DATE OF BIRTH	19 June 1990
PLACE OF BIRTH	Myanmar
INSTITUTIONS ATTENDED	University of Pharmacy, Mandalay, Myanmar
HOME ADDRESS	Nay Pyi Taw, Myanmar