Framing the challenge of poor-quality medicines:

problem definition and policy making in Cambodia, Laos, and Thailand

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Declaration

I, Marie Clémence Michelle Lamy, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Acknowledgements

Abbreviations

ACT	Artemisinin-based Combination Therapies
ADR	Adverse Drug Reactions
AEC	ASEAN Economic Community
AML	Antimalarial
API	Active Pharmaceutical Ingredient
AS	Artesunate
ASEAN	Association of Southeast Asian Nations
ASEAN ACTD	ASEAN Common Technical Dossier
ASEAN ACTR	ASEAN Common Technical Requirements
ASEAN PMAS	ASEAN Post-Market Alert System
ASEAN PPWG	ASEAN Pharmaceutical Product Working Group
ATM	Access to Medicines
BDN	Bureau of Drugs and Narcotics, Thailand
BFDI	Bureau of Food and Drug Inspection, Lao PDR
BMGF	Bill and Melinda Gates Foundation
BREMERE	Building Regional Expertise in Medicines Regulation, Information-sharing, Joint Investigation and Enforcement
BVBD	Bureau of Vector-Borne Diseases, Thailand
CBHI	Community-Based Health Insurance
CMPE	Center for Malaria Parasitology and Entomology, Lao PDR
CNM	National Centre for Parasitology, Entomology and Malaria Control, Cambodia
CoE	Council of Europe
CoRE	Centre of Regulatory Excellence
CPU	Consumer Protection Unit
CUST	Customs
DCD	Drug Control Division, Thailand
DDC	Department of Disease Control
DFAT	Australian Department of Foreign Affairs and Trade
DFF	Department of Drug and Food, Cambodia
DMS	Department of Medical Sciences, Thailand
EAASM	European Alliance for Access to Safe Medicines
EAS	East Asia Summit
ERAR	Emergency Response to Artemisinin Resistance
EU	European Union
FCTC	Framework Convention on Tobacco Control
FDD	Food and Drug Department, Lao PDR
FDQCC	Food and Drug Quality Control Centre, Lao PDR
GF	Global Fund to Fight Aids Tuberculosis and Malaria
GMP	Good Manufacturing Practices
GMS	Greater Mekong Subregion

GPHF	Global Pharma Health Fund
GPO	Government Pharmaceutical Organization, Thailand
HDI	Human Development Index
HEF	Health Equity Funds
HICs	High-Income Countries
HIV-AIDS	Human Immunodeficiency Virus Infection - Acquired Immune Deficiency Syndrome
HSP	Health Strategic Plan
ICT	Information Communication Technology
IFPMA	International Federation of Pharmaceutical Manufacturers Associations
IMC	Inter-Ministerial Committee to Fight against Counterfeit and Substandard Medicines, Cambodia
IMPACT	International Medical Products Anti-Counterfeiting Taskforce
IRACM	International Institute of Research Against Counterfeit Medicines
INT	Interpol
IOs	International Organisations
IP	Intellectual Property
LMICs	Low-Middle Income Countries
LMIS	Logistics Management Information Systems
LOMWRU	Lao-Mahosot Oxford Tropical Medicine Research Unit
LSHTM	London School of Hygiene and Tropical Medicine
MCs	Malaria Clinics
MERS	Middle Eastern Respiratory Syndrome
MICT	Ministry of Information and Communication Technology, Thailand
MMPs	Mobile-migrant populations
MoC	Ministry of Commerce
MoD	Ministry of Defence
MoE	Ministry of Education
MoEF	Ministry of Economic and Finance
MoH	Ministry of Health
MoI	Ministry of Interior
MoInfo	Ministry of Information
MoJ	Ministry of Justice
MoPH	Ministry of Public Health, Thailand
MoU	Memorandum of Understanding
MoY	Ministry of Youth
MPs	Malaria Posts
MPSC	Medical Product Supply Center
MQ	Mefloquine
MSH	Management Sciences for Health
NOMCOL	Network of Official Medicines Control Laboratories
NCDs	Non-Communicable Diseases
NEML	National Essential Medicines List
NGOs	Non-Governmental Organisations

NHPCV	National Centre for Pharmacovigilance, Thailand
NHQC	National Health Products Quality Control Centre, Cambodia
NHSO	National Health Security Office, Thailand
NMRA	National Medicines Regulatory Authority
NOMCOL	Network of Official Medicines Control Laboratories
oAMTs	Oral Artemisinin Monotherapy
PEPFAR	President's Emergency Plan for AIDS Relief
PFSCM	Partnership for Supply Chain Management
PMS	Post-Marketing Surveillance
POL	Police
PPHOs	Provincial Public Health Offices, Thailand
PPM	Public Private Mix
PQM	Promoting Quality of Medicines
PR	Principal Recipient
PreMA	Pharmaceutical Research & Manufacturers Association, Thailand
PSI	Population Services International
PV	Pharmacovigilance
RAI	Regional Artemisinin-resistance Initiative
RDTs	Rapid Diagnostic Tests
SARS	Severe Acute Respiratory Syndrome
SFs	Substandard and Falsified Medicines
SIDA	Swedish International Development Agency
SMP	Safety Monitoring Program
SOP	Standard Operating Procedures
SSFFCs	Substandard/ Spurious/ Falsely-Labelled/ Falsified/ Counterfeit Medicines
TFDA	Thai Food and Drug Administration
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UHC	Universal Health Coverage
UNODC	United Nations Office on Drugs and Crime
USA	United States of America
USAID	United States Agency for International Development
USP	United States Pharmacopeia
VHW	Village Health Worker
VMW	Village Malaria Worker
WB	World Bank
WHA	World Health Assembly
WHO	World Health Organisation
WHO RAS	WHO Rapid Alert System
WHO SEARO	WHO South East Asia Regional Office
WHO-UMC	WHO Uppsala Monitoring Centre
WHO PQ	WHO Pre-qualification System
WTO	World Trade Organization

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Abstract

Falsified and substandard medicines (poor-quality medicines) represent a pressing global health threat that necessitates a stronger policy response. They pose a considerable threat to human lives and an obstacle to infectious disease control, also due to the associated risk of antimicrobial resistance. Policy efforts against poor-quality medicines include strengthening national drug regulation systems and countering the illicit trade in falsified medicines. Current global policy endeavours to improve access quality medicines however form an array of initiatives rather than a coordinated global response. Since the 1990s, academics and policy actors recognise that the circulation of poor-quality medicines represents a pressing global public health concern. This has generated widespread debate in the literature on the drivers and determinants of this policy issue. While past studies highlight widespread disagreement on definitions of the problem of poor-quality medicines, the existing body of literature pays little attention to the way that the problem is understood among policy actors across national and institutional settings. This thesis seeks to explore varying interpretations of this problem among policy actors in three low and middle-income countries. It explores the role of ideas in policy processes by evaluating the variations in perceptions of the problem and the policy developments against poor-quality medicines. The problem of poor-quality antimalarial medicines in the Greater Mekong Subregion (GMS) offers an interesting case study. Despite notable national policy efforts against poor-quality antimalarial medicines in the GMS, evidence suggests that the problem of poor-quality antimalarials persists. As trade liberalization in the region intensifies, there are concerns that reduced custom controls and higher mobility of people and goods may cause further increase in this illicit trade. Through framing analysis, I analyse variations in perceptions of this threat across institutional and national settings. A social constructivist approach to policy analysis guides the analysis of interpretations of this problem and how these interpretations influence policy developments. This study then compares similarities and differences in framings of the problem and in policy processes across countries. I reflect on the dominant frames across the three case countries (the security, health systems and regulatory frames) and on the potential for policy coordination against poor-quality essential medicines in Southeast-Asia. To operationalize this approach, this study relies on three methods of data collection, namely; a stakeholder map, a document analysis and semi-structured interviews with key policy actors.

Chapter 1   Introduction

'Poor-quality medicines'[1] represent an important global public health challenge (Newton *et al.* 2011a). By definition, poor-quality medicines do not meet therapeutic standards set by national or international pharmacopeia [2], and contain either sub-optimal doses of the active pharmaceutical ingredient[3] (API) or no API, or may contain harmful ingredients which can lead to treatment failure or even death. There is evidence of poor-quality medicines across all drug categories, from lifesaving drugs such as antimicrobials to lifestyle drugs such as erectile dysfunction treatments or dieting pills (Karunamoorthi 2014). Poor-quality essential medicines are of particular concern as essential medicines satisfy 'the priority health care needs of a population', evidenced by disease prevalence and public health relevance (World Health Organization 2016a). Additionally, there are concerns that poor-quality medicines may contribute to antimicrobial resistance[4] (O'Neill 2016; WHO 2015). Poor-quality medicines therefore represent a real obstacle to infectious disease control worldwide.

1.1   Defining substandard and falsified medicines

The term 'poor-quality medicines' (Newton *et al.* 2010) here encompasses both *substandard* and *falsified* medicines (or SFs), as medicines that do not meet the therapeutic standards and therefore may pose a threat to health. A substandard medicine is a genuine drug (produced by either an innovator or generic manufacturer) that does not meet therapeutic standards, either due to a manufacturing error, poor storage conditions or other unintentional circumstances along the supply chain (World Health Organization 2010b). A falsified medicine (sometimes referred to as 'fake') is also substandard but is the result of criminal activity. This legal term proposed by Attaran and colleagues (2012) instead of 'counterfeit', encompasses the notion of 'intent to deceive' or wilful obliviousness of the perpetrator to the harm caused to patients

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[1] Medicine: a substance or preparation intended for the treatment or prevention of disease (Merriam-Webster's Learner's Dictionary n.d.). This thesis refers to medicines as either medicines or drugs interchangeably.

[2] Pharmacopeia: official reference standards published by governments on medicinal products with their formulas, methods of preparations, intended effects, and directions for use (United States Pharmacopeia 2011).

[3] Active Pharmaceutical Ingredient (API): 'Any substance or combination of substances used in a finished pharmaceutical product (or medicine), intended to furnish pharmacological activity or to otherwise have direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have direct effect in restoring, correcting or modifying physiological functions in human beings.' (World Health Organization 2011b, p.1)

[4] Poor-quality drugs with insufficient quantities of an Active Pharmaceutical Ingredient (API) may contribute to drug resistance due to low clearance of microorganisms (such as bacteria, parasites, bacteria or viruses). The microorganisms that survive then multiply rapidly and can create strains that are resistant to the drug (Morris & Stevens 2006; Park 2010).

by the poor-quality drug. In this thesis, I choose to avoid using the term 'counterfeit' so as not to reduce the debate to the intellectual property dimension of the problem (Kuehn 2013).

1.2   The policy problem of poor-quality medicines

The circulation in poor-quality medicines, which has reportedly taken place since the 1600s (Newton *et al.* 2010; Fernández *et al.* 2011), affects nations of all income categories and is exacerbated by globalization, the frequency of cross-border exchanges, and the presence of complex trading networks, making it a truly global health policy problem. While the problem of poor-quality drugs has reached a global scale and impact, it tends to be concentrated in regional clusters of countries characterized by intense cross-border movement, a high demand for cheaper drugs, and inadequate regulatory mechanisms. Since the 1990s, there has been growing attention towards the problem of poor-quality medicines within the global health community. In parallel, there has been an increasing amount of resources dedicated to regulatory strengthening to improve access to quality-assured medicines as stipulated under the Millennium Development Goals (goal 8) and the Sustainable Development Goals (target 3.8).

The mainstream policy response to the problem of access to poor-quality medicines is two-fold. It consists of both efforts to improve *access* to quality-assured medicines through the formal supply chain, as well as efforts to reduce the *illegal circulation* of poor-quality medicines. At the national level, National Regulatory Authorities (NRAs) are responsible for guaranteeing the quality, safety and efficacy of health products. NRA activities fall under two broad categories, including pre-marketing regulation (drug registration, licensing of manufacturing companies, of pharmacies, etc.) and post-marketing surveillance (pharmacovigilance[5], batch quality control, inspection of establishments, etc.) (WHO 2007). In addition to the role of NRAs, it has been suggested that efforts against the circulation of poor-quality medicines and to improve access to quality-assured medicines, require multi-sector cooperation at the national, regional and the global level. To illustrate this point, Table 21 (Appendix 1 page 301) summarizes the key global policy actors involved in policy making to reduce the circulation of substandard medicines. Despite growing global attention to the issue of poor-quality medicines, the problem persists. While there is limited systematically collected data to quantify the scale of the trade in poor-quality medicines globally (Kelesidis & Falagas 2015; Shah *et al.* 2015), the World Health Organization (WHO) suggests that a total

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[5] Pharmacovigilance: 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem' (World Health Organization 2004b, p.1)

of 30% of medicines in low-income settings are of poor-quality (IMPACT 2008). Additionally, the global market in poor-quality medicines is estimated to be between US$ 35 billion (Cockburn *et al.* 2005) and US$ 75 billion (WHO 2010).

1.3 Rationale

It is clear that the problem of poor-quality medicines transcends national borders (Hamburg 2015; The Lancet Editorial 2012; Seear 2012, 2013), yet there are few comparative analyses available on perceptions of the problem or the nature of policy responses across two or more countries. The literature suggests that while national efforts are insufficient to tackle such a complex cross-border threat (Seear 2013; Lee *et al.* 2015), the current global policy endeavours resemble an array of overlapping efforts with weak global leadership, rather than a coherent policy response (Mackey 2013). Despite efforts by the inter-governmental and donor organisations, such as the World Health Organization (WHO) and the United States Agency for International Development (USAID), to support global policy making to reduce the circulation of poor-quality medicines, these have had a limited impact on the capacity for NRAs to regulate pharmaceutical supply chains effectively. Moreover, cross-border coordination of efforts in response to the problem of poor-quality medicines remains limited. There is a gap in the literature as to why there is no effective, coordinated response although numerous studies point to the lack of a common agreement on the definition of poor-quality drugs as an impediment to a coordinated policy response (Khan et al. 2011; Dégardin et al. 2014; Newton et al. 2011b). Past studies on the policy problem of poor-quality medicines are predominantly normative in nature, highlighting the debate around this threat from an economic, socio-cultural, medical or political perspective (Karunamoorthi 2014; Dégardin *et al.* 2014; Wertheimer & Norris 2009; Fried 2011; Caudron *et al.* 2008; Bird 2007; Cahoy 2007; Outterson & Smith 2006). There is a shortage of empirical research analysing the policy implications of poor-quality medicines. Empirical work to understand the variations in how the policy problem is interpreted across national settings, can provide some explanation for the currently fragmented global policy response to the circulation of poor-quality medicines, which remains a threat to the health of populations.

1.4 Aims and Objectives

The aim of this thesis is to analyse and compare how the policy problem of poor-quality medicines is framed by policy actors across national settings. Four objectives guide this study:

1. Examine policy developments to reduce access to poor-quality medicines [6] in Cambodia, Laos and Thailand and evaluate the role of policy actors in shaping the policy process;

2. Explore how the problem of poor-quality medicines is framed by stakeholders across institutional settings in these three countries;

3. Compare the similarities and differences in framings of the policy problem across the three countries;

4. Discuss challenges and opportunities for cross-border policy coordination to reduce access to poor-quality medicines in Southeast Asia.

1.5   Case Study

One example of the cross-border problem of poor-quality essential medicines is the circulation of poor-quality antimalarials[7] (AMLs) in the Greater Mekong Subregion (GMS, also referred to as Mekong Region)[8]. Evidence indicates that the circulation of poor-quality AMLs in this region has been a key driver of artemisinin-resistance, creating further challenges to malaria control and elimination (Dondorp *et al.* 2004; White *et al.* 1999). The WHO and key experts from the Lao-Mahosot Oxford Tropical Medicine Research Unit (LOMWRU) were among the first to raise awareness in the late 1990s towards the regional challenge posed by poor-quality AMLs (Rozendaal 2001a; Newton et al. 2001; Newton et al. 2003), subsequently calling for international action against this problem and attracting international donor support (Newton *et al.* 2002). Appendix 2 page 303 summarises the evidence around the circulation of poor-quality medicines in the GMS.

Recent studies suggest that the prevalence of poor-quality AMLs in some Mekong countries has now declined[9], but poor-quality essential medicines remain a concern especially in remote rural areas (Tabernero, Newton, et al. 2014; Krech et al. 2014). The complex policy issue of poor-quality AMLs in the Mekong Region therefore provides a critical case to explore policy making in this area, including stakeholders' perceptions of the problem and how these may

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[6] and to improve access to quality assured medicines.

[7] Antimalarials (AMLs): A drug (including artemisinin-based combination therapy (ACTs)) intended for the treatment of malaria, a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes (World Health Organization 2017a).

[8] The Greater Mekong Subregion is a 'natural economic area bound together by the Mekong River', a regional construct named by the Asian Development Bank and commonly referred to as the GMS or the Mekong Region (Asian Development Bank n.d.). The Greater Mekong Subregion encompasses the following six countries and provinces: Cambodia, the People's Republic of China (specifically Yunnan Province and Guangxi Zhuang Autonomous Region), Lao People's Democratic Republic (Lao PDR), Myanmar, Thailand, and Vietnam

[9] Failure rates of AMLs in Cambodia have dropped from 7.4% to 0.7% between 2006 and 2011.

influence policy developments and programme implementation. Specifically, this study is structured around three neighbouring countries (namely, Cambodia, Laos and Thailand) that are faced with similar challenges, including evidence of poor-quality AMLs, the presence of unlicensed pharmaceutical outlets, and evidence of artemisinin resistance at border areas. All three countries share borders, are members of the Association of Southeast Asian Nations (ASEAN), have close-knit histories yet have different political and institutional systems and economies. While this thesis focuses on the case of poor-quality AMLs, respondents interviewed for this study frequently referred to the wider problem of poor-quality essential medicines. For this reason, the discussion of findings across the three countries extends beyond the problem of AMLs, to the wider problem of poor-quality essential medicines.

1.6   Approach

I adopt a social sciences approach to the study of a global health policy challenge. My study is anchored in social constructivism and based on the assumption that ideas play an important role in shaping policy processes. To study ideas, or the perceptions of policy actors, I use framing analysis. Frames are understood as a 'predominant mode of thinking and speaking about an issue' (Rein & Schön 1996, p.89). Frames are interpretations of a social phenomenon and a way of selecting information as an act of analysis or as an act of persuasion in politics (Rein & Schön 1996). While framing analysis has been predominantly used in the study of media representations, this thesis demonstrates the value of this approach in exploring how a problem is understood and defined in policy documents and by policy actors. I explore variations in framings across institutional and national settings, and analyse how different interpretations and perceptions may influence policy developments at the national and regional level. Frames are context-dependent and influenced by domestic political culture as well as global health narratives. For this reason, framings of an issue may vary between countries. I therefore compare the similarities and differences in framings of the policy issue and observe which frames are dominant across national settings. I then reflect on how each frame has been articulated differently across institutional and national settings, and discuss the implications of these frames for policy developments and for cross-border cooperation.

In this thesis, I refer to the health policy making process. This can be understood as the development of a health policy, from the emergence of a health policy issue within a policy community to the debate around the parameters of the policy problem, and finally to the policy solution or plan of action. Health policies[10] are defined as intentions to act and courses of

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[10] Policies can take the form of laws or policy guidelines.

action (and inaction) driven by a set of actors in a given context that affect the institutions, organizations and services in response to a health policy issue (Walt & Gilson 1994; Buse *et al.* 2005, p.6). For each case country, I explore how the 'issue' around poor-quality medicines as a policy concern emerges and how framings of this issue have triggered (or not) policy interest to address the problem of poor-quality AMLs. I do not seek to analyse the effectiveness of existing policies or to evaluate the success of their implementation. Instead, this study explores how policy changes occur over time, evaluates framings of the policy issue in different contexts and the implications of these framings for future policy development. I reflect on the similarities and differences in the policy processes in the three case countries and the opportunities for policy coherence to improve access to quality medicines in the region. This thesis argues for the need for more convergence in understandings and policy efforts against this regional and global health threat.

1.7   Thesis structure

The thesis is written in a monograph format and consists of nine chapters. It is structured in a manner that allows both an in depth understanding of each country situation, and paves the way for relevant discussion on the implications of framing in policy analysis, and on the potential for cross-border coordination to address the problem of poor-quality medicine in Southeast Asia. Following this introduction, Chapter 2 provides an overview of the policy debate on the problem of poor-quality medicines and its definition. Chapter 3 presents the results of a cross-disciplinary literature review on the determinants and the policy challenges linked to the issue of poor-quality medicines. In this chapter, I also identify the main thematic categories to explore during data collection and analysis. Chapter 4 details the analytical framework for this thesis and Chapter 5 details the methods I adopted to conduct my study. After a short section introducing the results from my fieldwork, chapters 6, 7 and 8 present the three case countries and the results of the analysis of policy processes and dominant frames among policy actors in Cambodia, Laos and Thailand respectively. Each results chapter begins with a brief introduction to the political, economic and health system context for each country. In chapter 9, I reflect on variations in framings and policy developments across the three national settings through a comparative analysis of the results. I discuss the dominant frames around the problem of poor-quality medicines and the implications of my research for policy developments and for cross-border policy coordination. I conclude this thesis with a short discussion of the limitations of this study, after which I offer suggestions for further research.

Chapter 2   The policy debate on poor-quality medicines

In this chapter, I explore the parameters of the policy debate around the problem of poor-quality medicines. Delineating the parameters of this debate is a first step towards understanding what is a complex policy problem. I outline the development of the normative discourse around poor-quality medicines as a policy problem since the 1990s, when it first received sustained attention at the global level. I then summarise the development of the debate around poor-quality medicines as a health policy problem, and the contribution of international stakeholders (including the role of global institutions[11]) in introducing 'access to quality medicines' (ATM) as a global policy goal. This chapter includes studies that focus on the problem of 'counterfeit', 'falsified', 'substandard', 'fake' or 'poor-quality' medicines, and that provide a wider understanding of this policy challenge encompassing trademark infringement and public health considerations.

2.1   The emergence of poor-quality medicines as a global health policy issue

The circulation of poor-quality medicines has gradually been recognised as a global health policy issue since the early 1990s. Both the WHO and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) have played a key role in gathering global support around the importance of improving access to quality and safe medicines, in the initial stages of the debate (WHO 1992). While the problem of poor-quality medicines is not new, the challenge of 'counterfeit' medicines was first addressed in the global health policy arena in 1985, at the Conference of Experts on the Rationale use of Drugs in Nairobi. The World Health Assembly Resolution WHA41.16 (1988) subsequently requested the initiation of programmes for the prevention and detection of 'falsely labelled, counterfeited or substandard pharmaceutical preparations' (WHO 1999). Since the 1990s, high-level meetings among global health institutions, debates among experts in pharmaceutical policy, legally-binding resolutions as well as non-binding declarations, have shaped and re-shaped the debate around poor-quality medicines. In 1994, a WHO Resolution (WHO 1994) followed the first international meeting on 'counterfeit' drugs held in Geneva (in 1992) by the IFPMA. This resolution was aimed at gathering cross-sectoral support to address the problem of poor-quality medicines (WHO 1999). In 1999, the WHO issued the first official recommendations on policy response to the circulation of 'counterfeit medicines' at the national level (WHO 1999).

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[11] A table summary of the global policy actors and their contribution to the ATM goal is available at Appendix 1 on page 301.

The WHO spearheaded guidelines to strengthen the regulation of pharmaceuticals. For example, the WHO pre-qualification (WHO PQ) system established in 2001, offers a comprehensive evaluation and certification mechanism for medicines to guide National Regulatory Authorities (NRAs) in their registration processes for new, quality-approved essential medicines. It provides a unified standard of acceptable quality, safety and efficacy across all medical products, and offers a comprehensive evaluation system and certification mechanism. The WHO PQ system also streamlines the pre-marketing quality control efforts for drug manufacturers, NRAs and donor organisations funding the procurement of essential medicines in low-middle income countries. The WHO PQ system was one of the first mechanisms aimed at improving access to quality medicines globally, and coincided with rising global awareness of the importance of guaranteeing the quality and safety of essential medicines. The WHO's subsequent initiatives reinforced its role in guiding policy efforts in this space. The Safety and Vigilance team at the WHO Essential Medicines and Health Products Department, for example, established the WHO Rapid Alert System (WHO RAS) to monitor poor-quality medicines. Through the WHO RAS, nation states are encouraged to share information globally about seizures of poor-quality medicines. Tabernero and colleagues (2014) note, however, that only 5-15% of member states regularly report seizures to the WHO.

2.1.1   Poor quality medicines as a trademark infringement

2.1.1.1   Intellectual Property law and trademark infringement

Since the problem of poor-quality medicines was first brought to the attention of the global health community by the WHO and IFPMA, the policy debate has changed in form and content. The problem of poor-quality medicines was first introduced as a trademark infringement before it was acknowledged as a public health issue (Clift 2010). The initial focus of the debate was on the infringement of Intellectual Property (IP) rights and the threat that this poses to pharmaceutical innovation and innovator brands, due to the diversion of profits to criminals (Outterson & Smith 2006). In addition to the WHO, other important policy actors influencing this development included the World Trade Organization (WTO) and the World Intellectual Property Organisation (WIPO) (Timmermans 2004). In response to the debate on the economic consequences of the trade in poor-quality medicines and the links with trademark infringement and IP protection, the WHO, the WTO and WIPO actively collaborated on surveillance and monitoring activities to understand the scale of the phenomenon. Poor-quality medicines were perceived first and foremost as a threat to the industry. Pharmaceutical companies regularly withhold information on evidence of falsified products from their brand, in order to safeguard the reputation of their products (Cockburn *et al.* 2005). The

pharmaceutical industry has advocated for tighter controls on patented products. Innovator pharmaceutical companies[12] have been accused of using actions against falsified medicines as a guise to target the generic industry, advocating for stronger laws against trademark infringement with definitions of 'falsified' medicines that can be interpreted broadly and risk impeding the ability of generic companies to produce cheaper versions of their branded products. This development is one illustration of how trade interests have traditionally prevailed over public health matters when it comes to the problem of poor-quality medicines (Blouin 2007; Bigdeli et al. 2012; Newton, Amin, et al. 2011; Liberman 2012).

2.1.1.2   Poor-quality medicines as 'counterfeit medicines'

WHO's definition of poor-quality medicines was initially centred on 'counterfeit medicines', defined as medicines that are deliberately and fraudulently mislabeled with respect to identity and/or source (WHO 1999). By referring to identity and/or source, this definition focuses predominantly on trademark infringement, classifying counterfeit medicines as copies of a branded product. This definition could inadvertently run the risk of encompassing generic medicines (non-branded and cheaper reproductions of an innovator drug), which could hinder access to more affordable generic medicines. This focus on trademark law could be attributed to the political influence of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS 1995) and the introduction of IP law to the international trading system, designed to preserve the rights of the innovator industries.

Most national laws since the 1990s also focus on IP protection for branded medicines, and fall short of addressing the pharmaceutical crime of falsified medicines (Newton, Amin, et al. 2011). The anti-drug-counterfeiting law introduced in Kenya in 2008 for example, was criticised as being drafted exclusively as a trademark concern, and thus posing a threat to the generic industry (Fried 2011; Cohn *et al.* 2013). In 2012, the World Health Organization (WHO) introduced the acronym SSFFCs (Substandard/ Spurious/ Falsely-Labelled/ Falsified/ Counterfeit) which encompassed all definitions of poor-quality medicines (WHO 2012). One shortcoming of this definition is that it amalgamated substandard, falsified and counterfeit medicines; all of which, however, would require distinct policy solutions. The definition has been revised to Substandard and Falsified medicines (SFs) following the recommendation of the WHO executive board (WHO 2017), with the aim of reducing confusion around the terminology.

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[12] Pharmaceutical companies investing in research and development of new drugs.

2.1.1.3   The limitations of intellectual property law

Global policy makers gradually realised that while protecting trademark infringements is important, a sole focus on IP law had important repercussions for access to affordable, quality medicines. IP law was seen as threatening access to cheaper quality medicines by erecting barriers to the production and trade of generic medicines, therefore creating a demand for more affordable medicines that counterfeiters exploit by offering cheaper alternatives of doubtful quality (Blouin 2007; Outterson & Smith 2006; Kamal, Smith & Tickell 2003; Ambroise-Thomas 2012; Karunamoorthi 2014; Pecoul *et al.* 1999). The shift in the debate coincided with the 2001 Doha Declaration on TRIPS and public health, and the introduction of flexibility mechanisms to the TRIPS Agreement. Paragraph 6 of the Doha Declaration established governance mechanisms for more inclusive trade that sought to expand access to medicines for LMICs lacking pharmaceutical capacity (WHO 2001). Such mechanisms included for example, Compulsory Licensing (CL), enabling governments to license domestic generic manufacturers to produce medicines without approval from patent holders for a royalty fee. Furthermore, policy makers gradually acknowledged the shortcomings of IP law, which fails to protect unbranded generic medicines prone to falsification. IP law cannot be used to prosecute falsified drug manufacturers operating under a bogus factory name, for example. International organisations such as Oxfam advocated for a shift in definition away from intellectual property law and more focused on improving national regulatory capacity for medicine quality assurance and control (Oxfam 2011).

2.1.2   Poor-quality medicines as a public health concern

2.1.2.1   Improving the affordability of medicines

Policy makers gradually noted the primacy of public health considerations over trade considerations with regards to the problem of poor-quality medicines. The debate shifted to encourage action by public health institutions to improve access to medicines (Newton *et al.* 2011; Akinyandenu 201). Arguably, the introduction of the Millennium Development Goals (MDGs) and Goal 8 (Target 8.E) on improving access to affordable medicines[13], played an important part in advocating for the need to improve access to quality, affordable medicines. Actors emphasized the need to protect the health of vulnerable populations, especially poorer communities, against cheaper poor-quality medicines in low and middle income countries (LMICs), where patients are disproportionately affected by the proliferation of poor-quality

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[13] MDG Target 8.E "to provide access to affordable essential drugs in developing countries".

medicines (Cahoy 2007; Caudron *et al.* 2008; Dorlo *et al.* 2012). It was gradually understood that the high price of genuine medicines, as well as the lack of public health insurance nets in LMICs, where patients rely predominantly on out-of-pocket payments for medicines, drove demand for cheaper medicines (Krech *et al.* 2014; Wertheimer & Norris 2009; Erhun *et al.* 2001; Akinyandenu 2013; Alfadl *et al.* 2013; Kelesidis *et al.* 2007; Glass 2014; Dégardin *et al.* 2014; Bird 2007; WHO 1999). This emphasis on the economic drivers of the demand for cheaper, poor-quality medicines and the trade barriers to access quality medicines, triggered international organisations such as Oxfam to steer the debate on improving access to *affordable* medicines. Oxfam and Médecins Sans Frontières through their 'Access Campaign' advocated for better access to affordable medicines (Medecins Sans Frontieres n.d.).

2.1.2.2   Access to Medicines beyond affordability

At the same time, in addition to the issue of affordability, stakeholders gradually acknowledged the need to consider other elements of the supply chain, when informing a policy response aimed at improving 'access to safe, effective, quality and affordable essential medicines and vaccines for all' [14]. Scholars concurred that the problem of poor-quality medicines goes beyond ensuring affordability and is intrinsically linked to the poor management of complex pharmaceutical supply chains and distribution networks (Buowari 2012; Burns 2006; Akinyandenu 2013; Erhun *et al.* 2001). At a consultative meeting held in 2000, the WHO and Management Sciences for Health (MSH) first introduced the '4As' (Availability, Accessibility, Acceptability, Affordability - see Figure 1 page 32) as a framework to illustrate the main supply chain dimensions of improving ATM (Center for Pharmaceutical Management 2003).

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[14] As stipulated in the Sustainable Development Goals (SDGs) target 3.8 in 2015.

Availability   Affordability

Accessibility   Acceptability
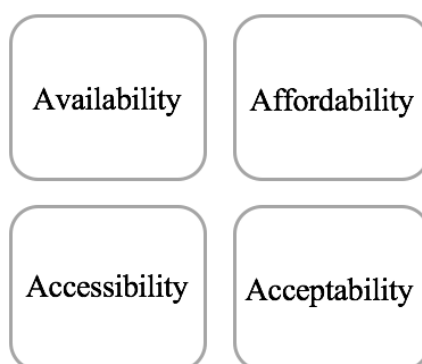
Figure 1 Access to Medicines Framework: The 4As by WHO-MSH (Center for Pharmaceutical Management 2003)

Availability relates to the upstream research, development, manufacturing (upstream availability), and the distribution of pharmaceutical products down the supply chain, from manufacturing establishments to pharmacy outlets (downstream availability). Under Accessibility, the WHO-MSH ATM framework highlights the importance of having pharmacy outlets geographically located within reach of patients. Affordability relates to the price of medicines. Finally, under Acceptability, the framework refers to the quality of medicines and the rational use[15] of medicines by patients, to ensure their safety and efficiency. Various iterations of this ATM Framework were subsequently developed[16]. In a publication entitled 'Equitable access to essential medicines: a framework for collective action' (WHO 2004a), the WHO introduced a revised framework which addresses supply chain constraints, as well as affordability and financing for medicines in four main categories (1. rational selection, 2. affordable prices, 3. sustainable financing, and 4. reliable health and supply systems), with considerations of quality assurance underpinning these four dimensions. This second ATM framework differs from the original WHO-MSH ATM framework, as it focuses predominantly on financing and the rational use of medicines and less on issues of accessibility. The last category of this framework only broadly encompasses constraints related to supply and demand of medicines. Beyond issues of supply and demand, stakeholders progressively acknowledged that the problem of poor-quality medicines was a wider health systems issue, related to access to health services, the state of health infrastructure and the political context.

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[15] The rational use of medicine requires that 'patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community' (World Health Organization 2015d, p.1)

[16] Another version of the ATM framework was developed later by Frost and Reich (2008). The Frost and Reich ATM framework (2008) is built around the 4As model and refers to Availability, Affordability but includes two different As, namely; Adoption (related to the demand for medicines) and Architecture (the international actors at play).

This shift was triggered by a key publication that will be detailed in the literature review (Chapter 3). Beyond the affordability of genuine medicines, stakeholders also realised the intrinsically global nature of the problem of poor-quality medicines.

2.2 Improving access to quality medicines as a global policy goal

2.2.1 A policy response against poor-quality medicines

Poor-quality medicines produced in one country can easily affect the health of patients in another. For this reason, the problem of poor-quality medicines has gradually been recognized as a global health threat, requiring a multi-level policy response adapted to the specificities of a national context, and that successfully address the cross-border determinants of the problem. In 2012, the WHO recognised the importance of efforts 'to prevent and control (and decrease) medicines with compromised quality, safety, and efficacy' (WHO 2012b). As described in the introductory chapter to this study, the policy response can be described as two-fold: 1) improving access to good quality medicines, and 2) tackling the illicit circulation of poor-quality medicines. Both responses address the problem of substandard and falsified medicines, although arguably a response to tackle the illicit circulation of poor-quality medicines needs to address the crime of medicine falsification; while the former focuses on strengthening pharmaceutical regulatory systems to monitor the quality of registered medicines on the market, and to reduce the production and circulation of substandard medicines.

2.2.2 National and global actors driving this policy response

Considering the nature of the problem of poor-quality medicines as a cross-border policy issue, it has been suggested that a successful response to improve access to good quality medicines and to strengthen drug regulatory systems involves an array of policy actors, across and beyond the national realm and the sole responsibility of NRAs. Several global and regional health institutions have been involved in steering the global policy response to address the problem of poor-quality medicines. With the 2006 Declaration of Rome, the WHO first established an International Medical Products Anti-Counterfeiting Taskforce (IMPACT)[17] between member state representatives to address the problem of poor-quality medicines. This mechanism was weakened by conflicting national interests and a flawed debate around the definition of 'counterfeit medicines', which was seen as impeding on the generics trade and thus on access to affordable medicines (Mackey 2013). By 2012, the WHO's Resolution WHA65.19

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[17] IMPACT was established as an inter-state mechanism spearheaded by representatives from the WHO member states to discuss the problem of poor-quality medicines within the WHO.

established the Member State Mechanism to replace IMPACT (WHO 2012b) and in 2014, resolution WHA67.20 agreed on at the 67th World Health Assembly, discussed the need to strengthen pharmaceutical regulatory systems to address the problem of poor-quality medicines.

Beyond the role of inter-governmental negotiations, the wider global health community including research institutions, industry associations and donor organisations, recognised the need to build stronger drug regulatory systems to address this issue with the help of technical agencies. International agencies, such as the United States Pharmacopeia (USP)[18], entered the scene at the beginning of the new millennium to strengthen the capacity of national pharmaceutical regulatory systems. USP has played an important role globally in improving the capacity of NRAs to monitor the quality of pharmaceutical products. Donor organizations and global health partnerships, including the Global Fund to Fight Aids, Tuberculosis and Malaria (GF), have also demonstrated an interest in promoting health systems strengthening to improve the regulation of pharmaceuticals and to support efforts against infectious diseases such as malaria. Through the Regional Artemisinin Initiative (RAI) announced in 2013 for example, the GF provides financial support to improve the regulatory capacity of NRAs in the Greater Mekong Subregion (GMS), and to ensure an adequate supply of quality ACTs. These efforts have contributed to reducing the circulation of no-longer recommended treatments to counter the growing threat of multi-drug resistant malaria.

2.2.3 International declarations on falsified medicines

Aside from the World Health Assembly resolutions, other non-binding declarations and conventions contributed to the international communities' growing technical knowledge around the policy goal of improving access to quality medicines. Global actors gradually acknowledged the complexity of reducing the circulation of falsified medicines specifically. As a result, several conventions and declarations were aimed at addressing the problem of falsified medicines as an internationally organized crime. The Medicrime Convention [19] drafted in 2011 by the Council of Europe (CoE), for example, was designed to provide law enforcers with a common legal framework to prosecute pharmaceutical crime (Mackey 2013).

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[18] USP is a non-profit organization providing technical support to nation states to improve national standards for monitoring the quality of medicines. USP operates sentinel sites with the use of the minilab, supporting the development of Standard Operating Procedures and working towards ISO certification for national pharmaceutical testing laboratories. USP also hosts a network of reference laboratories for medicine quality testing.

[19] Council of Europe Convention on counterfeiting of medical products and similar crimes involving threats to public health.

Its aim was to reinforce efforts against the intentional manufacturing of 'counterfeit' drugs. This convention guides lawmakers on how to address the crime of drug counterfeiting or falsification. The Medicrime Convention only entered into force in January 2016; however, to date there are still few signatories[20]. Regardless, the Medicrime Convention does reinforce the policy goal of ATM, adding to the body of existing conventions which can be applied to the crime of drug falsification[21].

The introduction of falsified medicines as a 'pharmaceutical crime' prompted the involvement of other organizations, including law enforcement agencies at the national (Customs and police officials at ports of entry or through the inspection of unlicensed drug outlets) and international level, including the United Nations Office for Drugs and Crime (UNODC) but also the International Criminal Police Organization (INTERPOL). UNODC, empowered by the Criminal Justice Resolution 20/6 (2011), is engaged in the global movement against poor-quality medicines, labelled 'fraudulent medicines' under its mandate to fight global organized crime. INTERPOL harnesses the skills and resources of police officials and customs officers in relevant countries through yearly operations to seize falsified batches and containers of poor-quality medicines. These activities are often reported in the media as 'success stories', and used to raise awareness about the circulation of poor-quality medicines, both among consumers and policy makers. Finally, The UNODC Model Legislative Provisions on Drug Control, adopted in 2016, were designed to guide member states' justice systems to legislate against pharmaceutical crime. These documents guide the reform of national legal frameworks in response to the problem of falsified medicines, although the extent to which they have been used and translated into national law is unclear. The conventions and resolutions around the problem of poor-quality medicines are part of the development of the policy goal of improving access to quality medicines.

This overview of how the problem of poor-quality medicines has emerged as a global health policy issue, provides an initial understanding of the evolving debate among policy makers. It also places the problem of poor-quality medicines within the wider debate around 'access to medicines', and introduces current efforts at the global level to reduce the circulation of SFs and improve access to quality medicines. The next chapter reviews the literature to discern how the problem is presented in academia.

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[20] 27 and 10 ratifications of the convention as of 2nd August 2018.
[21] Other conventions include the United Nations Office for Drugs and Crime Single Convention on Narcotic Drugs, or the Convention on Cybercrime 2001.

Chapter 3   Determinants of the trade in poor-quality medicines

In parallel to the policy debate described in Chapter 2, the problem of poor-quality medicines has been the focus of many studies. In this chapter, I review the determinants and drivers of the illicit trade in poor-quality medicines, as well as the challenges to forming a policy response, as presented in the literature. Past studies have served to raise awareness about substandard and falsified medicines as a global health policy problem (Sipahi *et al.* 2014). The majority of studies on poor-quality medicines to date focus on the medical and statistical aspects of poor-quality medicines and their circulation, providing information on the prevalence of poor-quality medicines from small batches of sampled medicines or describing the chemical content of tested samples (Liu & Lundin 2016).

In this review, I have included studies that refer to poor-quality, substandard, falsified or counterfeit medicines for a wider understanding of the challenge of poor-quality medicines. I examine studies across disciplines, beyond the purely medical and including papers written from an economic and legal perspective that describe the problem of poor-quality medicines, its determinants and challenges. In their recent study, Liu and Lundin (2016) provide an insightful review of the determinants, drivers and key challenges around the problem of falsified medicines. No single peer-reviewed study, however, offers a comprehensive analysis of these factors for both falsified and substandard medicines. Throughout this chapter, I present a list of key themes and sub-themes emerging from the literature. This list of themes can be used to guide research on the problem of poor-quality medicines from a policy perspective. The last section explains how the results of this literature review and the themes emerging from the literature, inform the conceptual framework for this thesis. I also reflect more broadly on the gaps in the literature that this thesis seeks to address.

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┌──────────────────┐
│  689 records     │
│  identified through│          ┌──────────────────┐
│  database search ├─────────▶│  130 duplicates  │
│  (MedLine, PubMed,│          │  removed         │
│  BASE and Global │          └──────────────────┘
│  Health)         │
└────────┬─────────┘
         │
         ▼
┌──────────────────┐          ┌──────────────────┐
│  559 records screened├─────▶│  302 records excluded│
│  by title and abstract│      │  (see exclusion  │
└────────┬─────────┘          │  criteria)       │
         │                    └──────────────────┘
┌──────────────────┐          
│  29 additional   │          
│  papers identified│    ┌──────────────────┐     ┌──────────────────┐
│  through manual  ├───▶│  286 records selected├──▶│  172 excluded from│
│  search          │    │  for full review │     │  full review     │
└──────────────────┘    └────────┬─────────┘     │  (not relevant to aim of│
                                 │               │  this review)    │
                                 ▼               └──────────────────┘
                        ┌──────────────────┐
                        │  114 studies included│
                        │  in thematic content │
                        │  analysis        │
                        └──────────────────┘
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Figure 2 Flow diagram on scoping of relevant studies

The papers analysed in this chapter were sourced from four databases: MedLine, PubMed, BASE[22] and Global Health. While the problem of poor-quality medicines is not a recent phenomenon, concerns about the health and economic implications of poor-quality medicines rose and attracted the attention of academia, the pharmaceutical industry and the World Health Organization (WHO) from the 1990s onwards. The body of literature on this topic is limited in size and the intention was to be as inclusive as possible. For this reason, date limits for this search were set from 1990-2016. The search was performed in January 2016, using the following key words in various combinations: (counterfeit OR fake OR falsified) AND (medicine* OR drug*). The search was limited to references published in English. The diagram above (see Figure 2, page 37) illustrates the scoping of relevant studies from this search. 689 records were initially identified through the database search and, after removing all duplicates, a remaining 559 records were screened by title and abstract for relevance. Below is a summary of the exclusion and inclusion criteria for the title and abstract review (see Table 1 on page 38).

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[22] BASE: A multi-disciplinary database which searches freely-available academic websites, including institutional online depositories, e-journal providers, and e-books.

Exclusion Criteria	Inclusion Criteria
News articles	Journal articles
Book reviews	Reports
Published before 1990	Opinion Editorials
Non-English	Books
No clear focus on health	Public health angle
Medical studies exclusively on prevalence rates of poor-quality medicines or on quaity detection methods.	

Table 1 Criteria for selecting articles for full review

A total of 114 studies published between 1991 and 2016 are included in this review. The list of studies is available in Appendix 3 on page 308. For this review, I identified key themes discussed by author(s) under which they describe the determinants, drivers and challenges linked to the problem of poor-quality medicines in various geographical settings. Through a thematic content analysis, I extract the 'reason' or explanation given by the author(s) as to why the trade in poor-quality medicines emerges or persists in various geographical settings. The reviewed papers point towards both factors *contributing* to the trade and discrepancies in *addressing* the problem, as factors that allow this trade to persist – both of which contribute to scaling up this phenomena to the global scale. The emerging themes from these studies were coded iteratively using Nvivo, and converged under three main thematic categories: the economic drivers of the illicit trade in poor-quality medicines; the socio-cultural determinants of the policy problem; and the legal and regulatory challenges to a policy response. The relevant sub-themes were tabulated under each thematic category. These themes are summarised in Table 2 on Page 39 and detailed later in this chapter.

Theme	Subthemes
Socio-economic drivers	Globalization and trade
	Demand and supply
	Consumer perception and awareness of risk
Health systems issues	Health service delivery and infrastructure
	Health-seeking behaviour
	Capacity and capability of NRAs
	Supply chain of pharmaceuticals
Legal and regulatory challenges	Definition of poor-quality medicine
	Laws and policies regulating medicines
	Organized crime
	Enforcement
	Politics and vested interests

Table 2 Issues around the problem of poor-quality medicines emerging from the literature review

3.1.1 Socio-economic drivers

3.1.1.1 Globalisation and trade

Various authors point to economic and trade factors as driving the trade in poor-quality medicines (Bird 2007; Cahoy 2007; Yao 2006; Worsley & Wong 2013). They argue that increased globalization, the movement of goods and people across borders and an emphasis on global trade interests, have contributed to the circulation of poor-quality medicines via transnational supply networks. Trade liberalization and the freer movement of goods, they argue, facilitate the international impact of pharmaceutical crime (Shah *et al.* 2015; Dégardin *et al.* 2014; Glass 2014; Newton, McGready, Fernández, *et al.* 2006). Free trade zones resulting in lower custom controls on exports, have been identified as a specific factor contributing to the trade in poor-quality medicines (WHO 1999; Bate 2012). These can circulate more freely through Singapore or Hong Kong, on their way from China or India for example, to other Southeast Asian nations where there is a higher demand for cheap medicines (Worsley & Wong 2013). The literature also suggests that globalization adds complex layers in the supply

chain of pharmaceuticals which may be exploited by criminals (Dégardin *et al.* 2014). Raw ingredients may be produced in one country, pills made in another, packaged in a third and sold in a fourth country or online (Kuehn 2013), making it difficult to trace the source of an illicit product (World Health Organization 2010a). Globalization has also increased instances of re-importation and parallel trade, creating further opportunities for poor-quality goods to infiltrate the legitimate supply chain (Ahmed 2013; Dégardin *et al.* 2014; Moken 2003). Re-importation of excess stock is considered dangerous when and if the products are altered or repackaged. Falsified goods, whose original version is registered in a country, can re-enter the market without being picked up by border control. Similarly, the parallel trade[23] of medicines is considered as one of the main threats in developed markets, such as the United States of America (USA) or the EU (Dégardin *et al.* 2014; Moken 2003).

3.1.1.2   Demand and supply

Cahoy (2007), in his economic study of the trade in counterfeit medicines, refers to the discrepancy between Higher Income Countries (HICs) and LMICs as the 'North/South divide', arguing that the problem of counterfeit drugs 'is vastly different in developed nations than it is in developing nations' (Cahoy 2007, p.411). The disproportionate effect of poor-quality medicines on LMICs is attributed to slow economic development affecting the demand for cheaper medicines, as well as to a lack of awareness of the risks posed by falsified medicines or to different perceptions of quality. The literature suggests that this demand for cheaper medicines creates an exploitable business opportunity, with the production and supply of falsified medicines representing a profitable venture and attracting criminal organizations (Chaudhry & Stumpf 2013; Outterson & Smith 2006; Park 2010). Substandard and falsified medicines are reportedly sold at a cheaper price through official and unofficial channels after being stolen or diverted or produced at a lesser cost. Additionally, in his book on the global trafficking of poor-quality medicines, Bate (2012) argues that the price differential between genuine and falsified medicines is one of the main reasons why falsified drugs enter a market, as illustrated by the case of Russia during the economic crisis of 1997, when the demand for cheaper medicines was high.

High profits on the production of poor-quality medicines is one clear incentive for criminals to falsify medicines. These high profit margins may be explained by the fact that counterfeiters avoid costs related to research and development activities or licensing, that are normally

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[23] Parallel trade occurs when governments allow the trade of patented products across borders without the permission of the patent holder due to significant price differentials.

factored into the innovator brand's selling price, using cheaper raw ingredients in the fabrication process instead (Liang 2006; Dégardin *et al.* 2014; Park 2010). Dégardin *et al.* (2014) refer to the existence of large pharmaceutical manufacturing hubs in emerging economies such as China and India, where the workforce is cheaper and production costs are lower, allowing the production of cheaper medicines. It is also suggested that such sites may attract counterfeiters who are able to find genuine products in nearby factories as models to replicate (Yao 2006; Cahoy 2007), therefore facilitating the production of falsified goods in such settings. An additional challenge identified in the literature is new technology, the web, and how it facilitates the trade in poor-quality medicines. Cheap medicines made readily available online, is a growing global trend that attracts patients particularly in developing countries, where most consumers have ready access to the internet (Sipahi *et al.* 2014).

3.1.1.3   Consumer perception and awareness of risk

Various authors allude to a society's perception and attitude towards counterfeit products as a driver of this trade. Understanding the 'temporal, social and psychological conditions' that influence the consumer, is essential to explaining the determinants of the demand (Bird 2007, p. 388). One factor thought to influence consumer's willingness to buy a counterfeit product is the perceived quality (Bigdeli *et al.* 2012) and the perceived similarity of the counterfeit to the genuine product (Bird 2007). This is relevant in the case of fake drugs, as patients that see no difference between one or the other, sometimes due to the lack of information about the product, and may therefore buy the counterfeit drug – which is likely to be cheaper – out of economic necessity. Yao (2006) suggests that consumers, as rational decision makers seeking economic benefit, would therefore choose to obtain the same product at a better value, the cheaper medicine also more likely to be counterfeit. While such insights are helpful, most studies addressing consumers' perceptions focus on LMIC settings and rarely account for consumers' attitudes to poor-quality medicines in HICs.

Some authors also argue that a general lack of awareness of the risks of purchasing medicines from unlicensed outlets, means that the less educated and often poorer communities are the primary victims of this trade (Sawminath 2008; Kelesidis and Falagas 2015; Siphali *et al.* 2014; Glass 2014; Krech *et al.* 2014). Additionally, the perceived scarcity or lack of access to the genuine product in licensed outlets, provides an additional reason for the consumer to purchase it from alternative outlets, even if unlicensed (Eisend and Schuchert-Guler 2006). Attitudes and perceptions have a direct influence on consumer behavior towards fake products in general, including fake drugs. Patients buying a fake drug may knowingly believe that the

harm they incur from the fake product, may be less than the harm incurred from not taking any medication (Bird 2007; Gaudiano *et al.* 2007). Further studies suggest that a higher income and higher levels of education have a negative impact on one's willingness to buy counterfeit products (Alfadl *et al.* 2013). Yao (2006) further argues that by heightening consumer awareness, the demand for fake drugs would subside. In a study on the purchase of fake Tylenol (a painkiller), however, it was found that neither the perceived legal risk nor the societal consequences influence the intent of the participants to buy this counterfeit good (Bird 2007). This may be explained by the fact that Tylenol is not a lifesaving drug and, thus, the consequences incurred if it was not efficacious are considered minimal.

3.1.2   Health systems issues

3.1.2.1   Health service delivery and infrastructure

The literature on poor-quality medicines also demonstrates the need to focus on wider health systems strengthening in order to improve access to quality medicines (Newton *et al.* 2011).

> Access to medicines and medicine quality are two sides of the same coin...The problems of poor quality medicines cannot be viewed in isolation, as they are enmeshed with many other complex health system problems, especially the affordability and accessibility of medicines and the (often limited) capacity of Medicine Regulatory Authorities [NRAs] (Newton *et al.* 2011, p.3)

The literature argues that weak health systems and drug regulatory capacity fuels the circulation of poor-quality medicines. Some argue that weak health service delivery in general and poor health infrastructure, may render access to quality pharmaceuticals difficult and encourage the trade in poor-quality medicines through alternative channels (Hosseini *et al.* 2011). It is suggested that the presence of poorly trained health workers with a lack of vigilance or awareness about the origin and quality of medicines they dispense, create risks of poor-quality medicines going undetected even in the formal, public health sector (Chika *et al.* 2011; Khan, Okumura, *et al.* 2011). Weak health systems and poor health infrastructure may engender a lack of trust in the public health sector *(Brhlikova et al.* 2011), and encourage patients to seek treatment in alternative unlicensed outlets where poor-quality medicines are more likely to be found and distributed, thereby encouraging the trade (Bigdeli *et al.* 2012; Liang 2006; Aldhous 2005; Dégardin *et al.* 2014; Karunamoorthi 2014; Bate 2012; Tipke *et al.* 2008; European Alliance for Access to Safe Medicines (EAASM) 2008).

3.1.2.2   Health seeking behaviour

Individual preferences shaped by socio-cultural constraints influence general health seeking behaviour and might further explain why a patient may end up buying a counterfeit drug (Bigdeli *et al.* 2012). This was illustrated by Lalani and colleagues (2015) in the case of Afghanistan, where patients seek treatment from the private sector and often purchase medicines from private outlets (including unlicensed outlets), where lower regulations mean a greater risk of obtaining medicines of poor-quality. The tendency to self-diagnose and self-medicate could be explained by patients' higher levels of trust towards friends, relatives and neighbors selling medicines, rather doctors and pharmacists (Bird 2007; Alfadl, Ibrahim, *et al.* 2013). Patients in more remote areas with no access to a public health facilities or pharmacies, may feel more inclined to buy their medication from the local store which might also be selling drugs (without a license to do so). Moreover, some authors point to the risks of dispensing medicines in plastic bags or as a cocktail of drugs (Yuk *et al.* 2015; Gaudiano *et al.* 2007), as this removes the possibility to verify the nature and quality of the medicines or its packaging and to consult treatment recommendations. Others argue that the irrational use and over-prescription of medicines may lead to shortages in the public sector, and create a gap in the market that counterfeiters can thereafter exploit (Bigdeli *et al.* 2012; Bate 2012). The literature suggests that health-seeking behaviour has an impact on access to medicines, thereby favouring the trade in poor-quality drugs.

3.1.2.3   Capacity and capability of NRAs

The literature also argues that LMICs are generally faced with a lack of financial and human resources to tackle the problem of poor-quality medicines, leading to poor capacity within NRAs for the regulation of pharmaceuticals (Karunamoorthi 2014; Aldhous 2005; Ahmed 2013). Kelesidis and Falagas (2015) argue, for example, that inadequate resources and expertise makes it challenging for some NRAs to establish stringent Good Manufacturing Practices (GMP) for the domestic pharmaceutical industry. Another consequence of inadequate resources within NRAs is the lack of well-equipped national laboratories as medicine quality testing facilities[24] (Nayyar *et al.* 2015; Bate *et al.* 2009). NRAs may also be weakened in their operations without the appropriate mandate to carry out random controls, to confiscate stocks from unlicensed outlets, to close down illegal outlets, or even to arrest presumed counterfeiters (Aldhous 2005; DeKieffer 2006; Caudron *et al.* 2008; Bigdeli *et al.*

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[24] Laboratories are not always ISO 17025 certified, an accreditation which guarantees that the right procedures are in place for testing health commodities.

2012; Liberman 2012). The lack of resources might also affect their capacity to operate high-end laboratories and to implement the screening technology required to screen fake drugs (Bate et al. 2008; Mukhopadhyay 2007; Johnston & Holt 2014; Lalani et al. 2015; Andreotti 2005; P. Newton et al. 2008). Additionally, authors argue that the technology is not up to date, or if it is available in the field (such as the hand-held CD3 or the mini-lab scan to test the quality medicines) it is unaffordable for NRAs with meagre resources (Marini et al. 2010; Wertheimer & Norris 2009). The literature argues therefore that NRAs alone are ill-equiped to tackle a problem of this scale.

3.1.2.4 Complex pharmaceutical supply chains

Authors acknowledge the complexity of the legitimate drug supply chain and the challenges of proliferating unlicensed drug distribution networks (Kelesidis & Falagas 2015; Krech *et al.* 2014). It is argued that unlicensed pharmacy outlets (beyond the jurisdiction of the NRAs) are most likely to sell poor-quality drugs (knowingly or not). It is through this grey market that criminals make most profits on their falsified drug batches (Akinyandenu 2013; Edwards 2011). Studies add that unlicensed drug outlets are often operated by untrained drug sellers who provide vague treatment recommendations, possibly encouraging irrational drug use, and who are unaware of the quality or health implications of the products they sell (Erhun *et al.* 2001; Foster 1991; Aldhous 2005; Palafox *et al.* 2014; Bigdeli *et al.* 2012; Buowari 2012). Palafox and colleagues (2014) describe the case of AMLs in Southeast Asia, where unlicensed outlets might encourage patients to purchase no-longer recommended Oral Artemisinin Monotherapies (oAMTs) as a malaria treatment instead of the recommended ACTs, because those are cheaper and still available through informal supply chains. The unregulated distribution network fuels the trade in poor-quality medicines as stocks of medicines sold in unlicensed outlets are sometimes stolen batches of medicines that could be substandard or falsified. As Gaudiano and colleagues (2007) point out, poorer patients have no choice but to obtain their medicines from these unlicensed outlets, either for financial reasons or because they are constrained by issues of accessibility to licensed outlets.

As well as physical unlicensed outlets, the literature argues that the rise of unlicensed internet pharmacies, adds to the risk of poor-quality medicines infiltrating both the legal and illegal supply chains (Dégardin *et al.* 2014; Ahmed 2013; Smith *et al.* 2014; Feldschreiber 2009). The proliferation of e-pharmacies is a cause for concern, as many are not licensed to sell medicines and their stocks are not quality-controlled and could therefore be of poor-quality. The trend of buying medicines online is seen as easy, speedy and convenient (EAASM 2008; Sipahi *et al.*

2014). Two studies point to the low cost and time investment for setting up a website and the effective e-commerce marketing strategies that make online pharmacies a profitable affair (Mackey & Liang 2011; EAASM 2008). Traynor (2010) explains that online pharmacies add to the complexity of the supply chain by blurring the source and trajectory of products, and selling medicines directly to both patients and healthcare professionals. Moken (2003) cites the example of fake Viagra produced in Chinese factories but sold via online wholesalers in Nevada and Colorado in 2002. Mackey and Liang (2011) estimate that 96% of online pharmacies are unlicensed. It is argued that unregulated online pharmacies are the main vector through which poor-quality medicines have reached higher income markets, where consumers have regular access to the internet (Liu & Lundin 2016; Kuehn 2013).

Poorly managed and complex supply chains for medicines increase the health system's 'vulnerability to substitution of diverted products', providing an outlet for the illicit trade in poor-quality medicines (DeKieffer 2006, p.344). The complexity of medicine supply chains may also arise from the high number of intermediaries in a typical pharmaceutical supply chain (DeKieffer 2006; World Health Organization 1999; Ahmed 2013; Gostin *et al.* 2013; Khan, Okumura, *et al.* 2011; Young 2004; Christian *et al.* 2012; Vastag 2003; Palafox *et al.* 2014). A higher number of entry points along the supply chain, allow counterfeiters to infiltrate poor-quality products or to repackage medicines and replace genuine ones with falsified batches (Akinyandenu 2013; Hamburg 2015; Rudolf & Bernstein 2004). At all stages in the production and supply chain, from raw material to the patient, products can be stolen or diverted and evidence of falsification can be ingested, making it difficult for anyone to pinpoint the fraud (DeKieffer 2006; EAASM 2008). Bate (2012) cites the example of Coartem (an AML treatment produced by Novartis) batches diverted from the airport in Angola between 2008 and 2011, leaving 534,000 patients without treatments. DeKieffer (2006) adds that counterfeiters can 'salt' shipments with their falsified drugs and can easily replace license documents while going unnoticed. These complex distribution channels make it difficult to identify the source of manufacture of a given product and to verify its quality (Wertheimer & Norris 2009; Rudolf & Bernstein 2004).

Others add that globalisation and the sheer number of brands on the global market, has made it even more difficult to know which manufacturers, distributors or products can be trusted (Nsimba 2008; Newton, McGready, Fernandez, *et al.* 2006; Liu & Lundin 2016). The increasing complexity of pharmaceutical supply chains are made up of various 'decision points' which are all arguably susceptible to corruption (Cohen *et al.* 2007). Corruption in the pharmaceutical sector can take the form of forging license documents, diverting donated drugs,

or even bribing officials and health professionals (Cockburn *et al.* 2005; Mackey & Liang 2012). It is estimated that billions of dollars are lost annually to corruption and fraud in the global health sector (Mackey & Liang 2012; Wertheimer & Norris 2009).

3.2   Challenges of a response to poor-quality medicines

This literature refers to key legal and regulatory constraints to policy reforms aimed at improving access to quality medicines and reducing the circulation of poor-quality ones. These legal and regulatory issues pertain to both national and global policy and legal frameworks and should be studied in context. A thorough understanding of these challenges, as presented in the literature and summarised in this section, is crucial to understanding why the problem of poor-quality medicines persists.

3.2.1   Legal & regulatory challenges

3.2.1.1   No common definition and an uncoordinated policy response

The definition of poor-quality medicines has been a cause for debate for over a decade (Fried 2011; Liberman 2012; Clift 2010). Despite the contributions of various international organizations to policy efforts against poor-quality medicines, the global response remains fragmented, with no clear leadership (Mackey 2013; Bigdeli *et al.* 2012; Mackey & Liang 2013). This, the literature argues, is partly because of the lack of a common definition and understanding of poor-quality medicines among these institutions, both in national laws, in policies and guidelines for NRAs, or across international institutions (Attaran, Barry, et al. 2012; Newton, Amin, et al. 2011). Policy actors frame the problem of poor-quality medicines differently across national and institutional settings, and this, authors argue, is as an impediment to coordinated cross-border action (Newton, Green, *et al.* 2011; Dégardin *et al.* 2014; Alfadl, Ibrahim, *et al.* 2013; Clift 2010; Park 2010; Bate 2012; Seear 2013; Fried 2011; Attaran *et al.* 2011; Mackey *et al.* 2015; Worsley & Wong 2013; Newton *et al.* 2014; DeCola 2010; Khan, Akazawa, *et al.* 2011; Glass 2014).

The literature is also divided on the terminology around poor-quality medicines. For example, in an economic study of drug counterfeiting, Cahoy (2007) suggests that one way to avoid confusion is to only label 'counterfeit' drugs that are produced out of an intentional act of deception, and frame others as mere IP infringements. Attaran and colleagues (2011), on the other hand, argue that the legal term of 'falsified' drugs fits more adequately with cases of pharmaceutical crime where the *intent to deceive* is present, while cases of drug

'counterfeiting' fit under IP law exclusively. Furthermore, authors note that the notion of 'intent to deceive' mentioned in the legal definition of falsified medicines above and which differentiates a criminal act of drug falsification from a trademark infringement is hard to prove legally (Hall, Newton, Green, Veij, et al. 2006; Newton, Green, et al. 2011). A clear demarcation between falsified and substandard medicines is therefore hard to discern in practice[25], making it challenging for law and policy makers to devise adequate and robust regulatory frameworks, knowing that falsified and substandard cases would require different legal and regulatory solutions (Newton, Amin, *et al.* 2011; Zhang & Zhang 2014). For some authors, the lack of a common definition also creates challenges for homogenous data collection and information sharing on the global prevalence of poor-quality medicines (World Health Organization 2010a; Shah et al. 2015; Glass 2014; Kelesidis & Falagas 2015).

3.2.1.2   Inadequate laws and policies for the regulation of medicines

The literature discusses the shortfalls of current national pharmaceutical regulatory frameworks, most of which focus primarily on trademark protection and fail to address the cross-border organized criminal threat of falsified medicines. As mentioned in the first comprehensive WHO report published on the threat of poor-quality medicines (WHO 1999), one main challenge to addressing the problem is the general lack of adequate, targeted national and international laws and policies to regulate against poor-quality medicines, and the crime of medicine falsification in particular. Firstly, it is estimated that only 20% of all WHO member states have well-developed pharmaceutical regulatory frameworks (Jack 2012), with the remaining 80%, weakened by poor management of the supply chain of pharmaceuticals and heightened risks of both substandard and falsified medicines reaching patients. The literature argues more specifically that NRA's capacity to register priority medicines rapidly or their pharmacovigilance and post-marketing surveillance capacity, remains weak (Nwokike *et al.* 2013).

Another viewpoint from the literature is that discrepancies between, as well as within, national regulatory frameworks and the lack of cooperation between national stakeholders, are detrimental to a policy response to reduce the circulation of poor-quality medicines (Newton, McGready, Fernandez, *et al.* 2006; Shah *et al.* 2015; World Health Organization 1999; Blouin 2007; Newton, Green, *et al.* 2006). Authors imply that cooperation between health policy makers, police and customs officials, health professionals, the pharmaceutical industry, and

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[25] There is undeniably some overlap between falsified and substandard medicines (Seiter 2009) and it is essential to consider both in parallel; as 'poor-quality medicines'.

international organizations, is crucial yet not always regular and rarely institutionalised. The lack of a systematic and compulsory reporting system is yet another limitation to addressing this phenomenon (Cockburn *et al.* 2005; Newton *et al.* 2014). To illustrate this point, Newton and colleagues (2014) explain that when poor-quality batches of AMLs were seized in Angola in 2012, the issue was reported via Facebook to responsible authorities after a 5-month delay. Reporting and information sharing mechanisms are deemed essential, and Newton *et al.* (2014) argue that existing mechanisms such as the WHO Rapid Alert System (RAS) should be made mandatory in this respect.

Legal studies addressing the challenge of drug counterfeiting such as those published by Rierson (2007) and Rudolf & Bernstein (2004), suggest that current national legal frameworks pay more attention to penalizing the counterfeiting of other, more harmful products, such as counterfeit tobacco products, over falsified pharmaceuticals. In the few countries where penalties against the pharmaceutical crime of medicine falsification do exist, however, these are not commensurate to the severity of the crime and are disproportionately low when compared to those incurred by narcotics criminals (Akinyandenu 2013; Gautam *et al.* 2009; Hosseini *et al.* 2011; Chika *et al.* 2011; Liang 2006). Existing regulatory frameworks offer few legal deterrents against the falsification of medicines (Cahoy 2007; Outterson & Smith 2006; Chaudhry & Stumpf 2013; UNODC 2010; Mackey & Liang 2011; Buowari 2012; Nsimba 2008), making it an 'opportunistic crime' for which the financial rewards far outweigh the risks of prosecution (Interpol *et al.* 2008; Stevens & Mydin 2013; Gautam *et al.* 2009). Smith and colleagues (2014), in their account of the value of the EU Falsified Medicine Directive, add that no national regulatory framework against poor-quality medicines is complete without strong laws regulating the sale of medicines online as a rising threat, yet, they state that these are scarcely a part of national regulatory frameworks.

Studies concur that nations cannot tackle the threat of poor-quality medicines in isolation, and that inter-sectoral and cross-border cooperation is necessary to address this challenge (WHO 2010; Foster 1991). Authors add that an adequate policy response would require a shift from single to multipolar policy making, and from national to bloc policy level (Caudron *et al.* 2008; Gaudiano *et al.* 2007; Gastrow 2013). The literature also reports a lack of a coordinated global policy response to the issue of poor-quality medicines. Authors argue that no global framework to date successfully harnesses the expertise of all key institutions to steer a coordinated global policy response against the circulation of poor-quality medicines (Gostin *et al.* 2013; Mackey & Liang 2013). In their study of global efforts against 'counterfeit' medicines, Mackey & Liang (2011) argue that while the WHO may seem like an obvious global institution to

spearhead the fight against falsified medicines, it has been criticized for its inefficiency in leading the response against such a complex public health challenge. In his paper on the governance of poor-quality medicines, Mackey (2013) reviews the role of key global institutions around the problem of 'counterfeit' medicines, highlighting the discrepancies of WHO's role in guiding a global response. The same author proposes a new governance framework to address this issue, arguing that the UNODC is in the best position to guide policy making against the falsification of medicines. Authors note the absence of an international legal framework and a treaty to regulate on the issue of poor-quality medicines. They argue that this impedes the ability of policy actors to tackle this trend globally and to prosecute criminals across borders (Dégardin *et al.* 2014; Binagwaho *et al.* 2013; Newton *et al.* 2014). While international institutions to enforce IP laws, such as the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS, 2001), have been in place (Dégardin *et al.* 2014), a coordinated response against drug falsification as an organized crime is almost nonexistent (Bate 2012; Mackey & Liang 2011).

3.2.1.3   Complex organised crime

Various authors point out that medicine falsification is an organized criminal activity of a global nature, which is hard to dismantle because it is highly complex, often underground, and transcends borders and legal frameworks (Cahoy 2007; United Nations Office for Drugs and Crime 2010; Gastrow 2013; Andreotti 2005; Reynolds & McKee 2010; Gillespie & McBride 2013). Hosseini and colleagues (2011, p.166) illustrate the complexity of these organized criminal networks, and describe the case of Iran as a transit country for the narcotics trade and the trade of other illegal goods, including falsified medicines. Organized criminal groups have taken advantage of the technological advances and rapid methods of communication to run their businesses internationally (Dégardin *et al.* 2014; Ambroise-Thomas 2012; Gautam *et al.* 2009; Mackey & Liang 2011). The complexity of these networks makes it hard to track the criminals and arrest the culprits. According to the literature, the fact that criminal organizations involved in drug counterfeiting may also be linked with the narcotics trade only complicates the situation further, by blurring and expanding the supply chain networks for these poor-quality medicines (Dégardin *et al.* 2014; Aldhous 2005; Newton *et al.* 2002; Burns 2006). Moreover, it is believed that some groups have direct links with terrorist organizations such as Hezbollah or Al Qaeda, which facilitates access to a grey zone (a parallel economy such as the 'black market') (Bate *et al.* 2008; Liang 2006), where drug falsifiers can go undetected along the supply chain (Liu & Lundin 2016).

3.2.1.4   Enforcement capacity

Morris & Stevens (2006) argue that where laws and policies are in place, they are poorly enforced. The literatures suggests that the poor capacity of NRAs is one explanation for the poor enforcement of pharmaceutical management laws (WHO 1999; Johnston & Holt 2014; Yao 2006; Karunamoorthi 2014; Caudron *et al.* 2008; Kelesidis & Falagas 2015; Krech *et al.* 2014; Erhun *et al.* 2001; Rudolf & Bernstein 2004; Newton *et al.* 2006; Po 2001; Newton *et al.* 2011). One example cited by Skerrit and colleagues (2014), touches on the issue of poor-qualiy AMLs as evidence for bans against the production and distribution of oAMTs, are ineffectively enforced in the Asia-Pacific region, complicating efforts against unregistered, substandard or falsified AMLs in Southeast Asia. Weak rule of law and low prosecution rates are also attributed to poor training of the justice personnel, or poorly equipped law enforcement units (DeKieffer 2006; Chika et al. 2011). Without a consistently enforced legal framework, the prosecution rates remain low and low prosecution means no effective deterrent against pharmaceutical crime (Ahmed 2013; Gautam *et al.* 2009).

Morris & Stevens (2006) argue that the inability of patients to obtain redress for harmful products through civil liability mechanisms, is yet another contributing factor to the circualtion of poor-quality medicines, as civil liability clauses could discourage manufacturers from selling falsified drugs, or incentivise wholesalers to verify their stocks more thoroughly. According to Bate and colleagues (2009), discrepancies in enforcement within national legal systems represent a major challenge, as illustrated in the case of India where state regulation is often inconsistent with national (central) regulation. This means, for example, that drug manufacturers can seek registration in any Indian state where law enforcement is weaker. Bikoff *et al.* (2015) add that this discrepancy between central and federal enforcement, makes tackling a crime that respects no borders a difficult task. Various authors also point to the unfair consequences of double standards in drug export regulation, whereby products produced locally but intended for export are subject to a less stringent set of quality checks compared to drugs produced for local consumption (Chika *et al.* 2011; Caudron *et al.* 2008; Dégardin *et al.* 2014). This allows potentially poor-quality batches of medicines to reach countries with weaker regulatory systems without being detected.

3.2.1.5   Politics and vested interests

The literature argues that challenges linked to enforcing existing laws and policies, may be linked to the wider political system and the lack of accountability mechanisms, as well as

instances of corruption (Dyer 2014). The circulation of poor-quality medicines is a politically sensitive issue (Dégardin *et al.* 2014), and the literature suggests that weak regulation could be attributed to a general lack of political will, due to vested interests in the manufacturing or distribution of these medicines (Jack 2012; Burns 2006; Chika *et al.* 2011). Authors argue that governments have knowingly refused to act against counterfeiters out of 'willful ignorance' (Bate *et al.* 2008; Andreotti 2005), or for fear of seeing their country's reputation 'tarnished' by the public discovery and announcement of substandard drugs in their markets (Po 2001; Bate 2012; Cockburn *et al.* 2005).

Newton and colleagues (2014) suggest, however, that it seems illogical at whatever stage of national development not to prioritize stringent controls on costly products, such as pharmaceuticals that are so crucial to the welfare and the productivity of a population. The literature also argues that despite acknowledging the global challenges posed by poor-quality medicines, national stakeholders sometimes fail to recognize their responsibility towards the problem of poor-quality medicines (Sipahi *et al.* 2014; Amon 2008). Some may not acknowledge that the circulation of poor-quality medicines could be due to weak national pharmaceutical regulatory capacity within their borders, and instead shift the blame to neighbouring nations (Bate 2012). Besides a lack of political will to recognize part of their blame in this cross-border problem, policy makers and law enforcement officials may have direct vested interests in this trade, impeding the successful enforcement of existing laws (Akinyandenu 2013; Swaminath 2008; Bate 2012; Aldhous 2005; Bird 2007; DeKieffer 2006; WHO 1999).

Bigdeli *et al.* (2012) and Mackey & Liang (2012) add that in countries where public accountability is low and the social policy sector is not a priority, corruption can have an important impact on access to health services and medicines. Akinyandenu (2013) illustrates this point with the case of Nigeria, where corruption allows for the manipulation of regulatory procedures. Stevens and Mydin (2013) point to the difficulty of dealing with corruption, whereby more stringent penalties on drug counterfeiting could drive illegal activities further underground and encourage criminal groups to 'infiltrate law-enforcement agencies' for protection. Various authors refer to the case of China and explain that local government officials have been known to shelter such illegal activities under their watch, sometimes with the support of the People's Liberation Army in China, using their hospitals as distribution outlets for the falsified drugs (Lewis 2009; Bate *et al.* 2008; Zimmerman *et al.* 2014). Bird (2007) encourages us to look at the bigger picture however – illustrating that counterfeiting in China also represents an important source of employment in certain communities, which might

explain why efforts to enforce laws against these criminals are weak. Corruption and vested interest also act as a barrier to policy reforms to address the circulation of both substandard and falsified medicines.

3.3 Conceptual Framework for further research

The literature on poor-quality medicines represents an eclectic mix of studies from different disciplines that provide insights on the drivers, determinants and key concerns around this illicit trade. Through these combined insights, I note the complexity of what has been recognised as a global public health policy issue, and the emergence and development of the debate on 'access to medicines' as a policy goal. Based on this review, I reflect on the policy goal of improving access to quality medicines and how the themes described above can inform a conceptual framework for further research on the problem of poor-quality medicines as a public health concern. The list of themes emerging from the literature demonstrates the importance of considering health systems constraints, including health infrastructure and health seeking behaviour, as well as the socio-cultural fabric and political economy, to fully apprehend the complexity of the problem of poor-quality medicines in context. The literature also develops on the ATM framework first introduced into the policy debate by the WHO in 2000, to encompass more dimensions of access. Bigdeli *et al.* (2012) suggest that the main limitations of previous ATM frameworks[26] is that they were too linear, limited to supply chain constraints and focused solely on the pharmaceutical product rather than the patient. In response, Bigdeli *et al.* (2012) introduce a more dynamic ATM Framework, which incorporates a health systems approach to improving access *for all patients* (see Figure 3 below).

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[26] Such as the WHO-MSH (2000), the WHO (2004) and the Frost and Reich (2008).
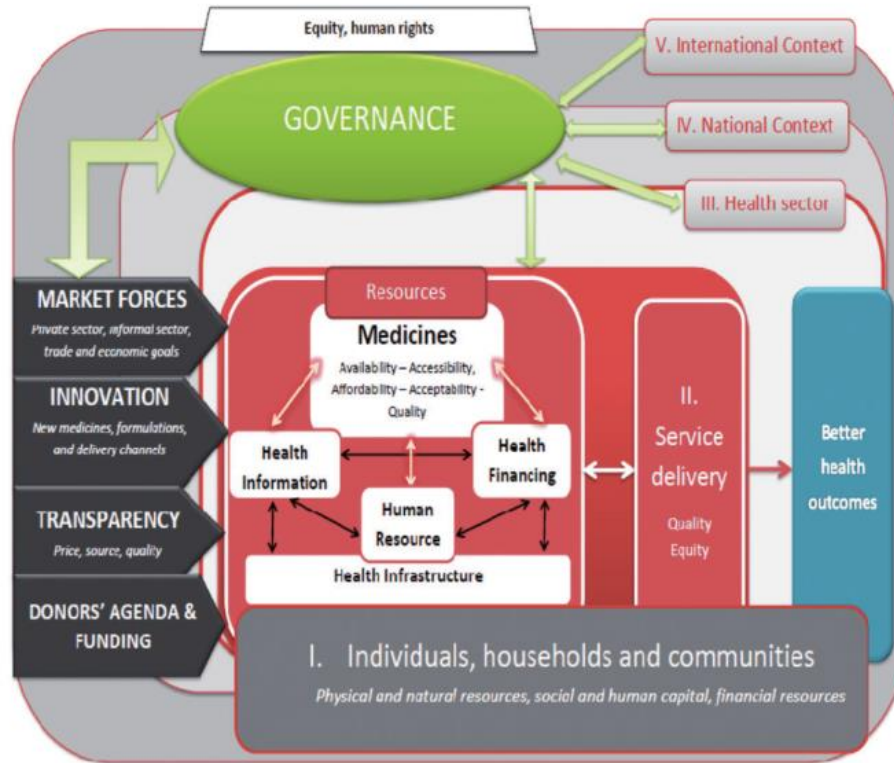
Figure 3 ATM from a health systems perspective (by Bigdeli *et al.* 2012)

This revised 'ATM from a health systems perspective' framework, reflects the complexity of considerations around ATM and the interaction between all systems constraints related to accessing medicines. The framework they propose includes five levels of constraints that impact access to quality medicines and reflects the dynamics of a systems approach to ATM, within which these constraints are inter-connected across the national, regional and global levels. While previous ATM frameworks acknowledged the role of international actors (e.g., in the 'Architecture' of ATM by Frost and Reich (2008)), Bigdeli and colleagues' framework goes a step further to recognize the impact of legal and regulatory constraints and the nature of national politics, as well as the influence of international donor agendas. It addresses the impact of the international and national economic landscape on access to medicines; referring, for example, to the challenge of globalization and the impact of economic development on ATM. Their framework also considers socio-cultural constraints affecting health systems (under 'individuals and communities'), such as health seeking behaviour. This framework recognises poor-quality medicines as a wider public health concern that can only be addressed by strengthening the health system at large.

The themes emerging from the literature review describing the determinants and challenges of the trade in poor-quality medicines, can be conceptualised within this ATM framework. For

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this thesis, I have adapted and simplified Bigdeli and colleagues' (2012) framework to encompass these themes (see Figure 4 page 54). The conceptual ATM framework proposed below offers a dynamic approach to understanding the problem of poor-quality medicines, in which I consider the national and global/regional context and its influence on the policy response to the problem of substandard and falsified medicines. This conceptual framework suggests that the supply and delivery elements impacting access (the 4As) should be considered within the wider health systems constraints, the health service delivery and health system architecture of a country. These health systems constraints are represented in the central black-coloured box as an inherent part of the national context. In light grey, I include the determinants and challenges related to access; the economic drivers (including pharmaceutical industry interests, globalisation and trade) that impact both the political context; as well as the socio-cultural factors that inform our understanding of the national context and explain the social constraints related to health service delivery. The legal and regulatory challenges to a policy response are also encompassed within this framework, and occur both at the global and the national levels.
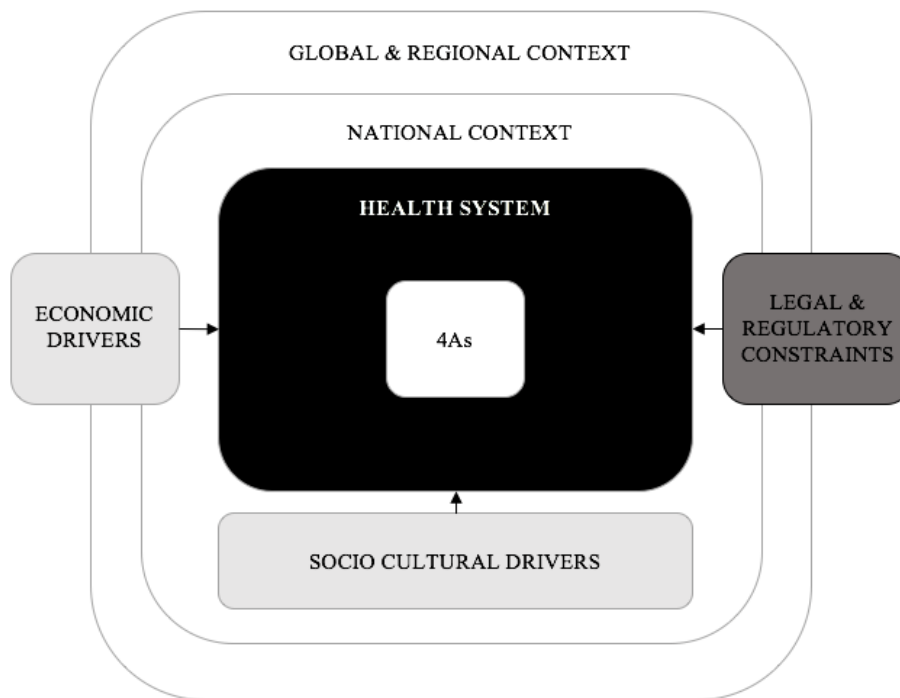
Figure 4 Access to Medicines Conceptual Framework

This conceptual ATM framework provides a systematic approach to understanding a complex phenomenon (the policy problem of poor-quality medicines) in context. It encourages a

reflection on all thematic elements contributing to the policy problem, while considering the nature of national politics and the socio-economic context of the country or region under study. An effective policy response to poor-quality medicines starts with a thorough understanding of the economic drivers, social practices and cultural factors that might impact the supply and demand for cheaper medicines, as well as the health systems constraints that impact the supply and delivery of quality pharmaceuticals and allow for poor-quality medicines to circulate. This conceptual framework informs the analytical approach for this thesis, which is aimed at addressing some of the main gaps in the literature that are outlined in the next section.

3.4   Research gaps

Four main observations can be made concerning the research gaps around the problem of poor-quality medicines. Firstly, despite noting the widespread disagreements on the definition of the problem of poor-quality medicines, there is a need for further research to understand how the problem is framed among policy actors. Secondly, there is an apparent lack of empirical research anchored in social sciences to explain interpretations of the policy problem of poor-quality medicines as well as to explain variations in policy pathways of response to improve access to quality medicines. Third, there is a need for comparative analyses of frames across borders to explain the challenges and opportunities for cross-border cooperation against poor-quality medicines. Finally, few studies have explored the problem of poor-quality medicines in an LMIC context, despite noting the disproportionate consequences of their circulation among vulnerable populations. This calls for further research on the problem of poor-quality medicines across LMIC settings.

3.4.1   Framing the problem of poor-quality medicines

Over half of the studies reviewed suggest that the lack of an agreed upon definition of the problem of poor-quality medicines is the main challenge to a coordinated policy response. The literature highlights the difficulty of differentiating between falsified and substandard medicines and proving the notion of 'intent' to guide policy response. For this reason, this thesis looks at both substandard and falsified drugs to understand the problem of poor-quality medicines all together. Beyond the choice of terminology, however, no studies explore the relationship between variations in perceptions of the problem of poor-quality medicines among policy actors and the variations in policy developments. The literature suggests that context and social norms impact stakeholders' understandings of what constitutes 'poor quality' (Alfadl, Hassali, *et al.* 2013). However, few studies to date have explored policy actors' perceptions of the problem across policy sectors and national settings. A few single-country

studies have previously explored global consumers' opinions of falsified medicines, as did Bird (2007) through an economic lens. Others have explored opinions of health care professionals (Ahmed 2013) or manufacturers and wholesalers (Khan *et al.* 2011) on the problem of poor-quality medicines. Finally, two single country studies on Sudan (Alfadl *et al.* 2013) and Nigeria (Erhun *et al.* 2001) explore a range of stakeholders' understandings, of the drivers and determinants of the illicit trade in poor-quality medicines and include policy actors in the sample of respondents. Neither of the two studies, however, offer an analysis of how policy actors' perceptions vary across institutional and national settings, and how these perceptions might affect policy coherence. Understanding variations in how the phenomenon is perceived across institutions and national settings can explain policy choices and variations in policy pathways of response.

Definitions of poor-quality medicines are seen as inherently socially constructed and it is implied that perceptions of the problem are likely to vary across institutional networks and across national borders. To understand the nature of these social constructions, empirical qualitative research into how the policy issue is framed is deemed appropriate. This justifies a closer examination of how policy actors present the issue, the factors they prioritize in their descriptions and the main challenges they identify over others – all of which provide some indication of their perception of this phenomenon.

3.4.2   Empirical research: analysing frames and policies process in context

The studies reviewed in this thesis are largely informed by a normative stance (Fried 2011; Caudron *et al.* 2008; Reynolds & McKee 2010; Wertheimer & Norris 2009; Christian *et al.* 2012; Dégardin *et al.* 2014; Glass 2014; Seear 2013). They provide a general delineation of the contributing factors to this trade, without providing in-depth accounts of this multi-faceted policy challenge and detailing why it persists in specific contexts through empirical research (Dégardin *et al.* 2014; Wertheimer & Norris 2009; Fried 2011; Caudron *et al.* 2008). Although these normative contributions are crucial to raise awareness among academia and policy actors about this health policy issue, there is a lack of in-depth empirical qualitative research on the topic (Liu & Lundin 2016). Many studies also review the scientific evidence on the prevalence of poor-quality medicines. However, there are few studies from a social sciences perspective that explore the determinants (economic, social, political and legal) of the problem of poor-quality medicines, in a given national or regional context (Karunamoorthi 2014; Christian *et al.* 2012; Kelesidis *et al.* 2007).

While the literature refers to numerous legal and regulatory challenges at the policy response against poor-quality medicines, few studies explore the national, regional and global policy efforts currently in effect to address this policy problem, or provide a thorough context-based analysis of where the policy and regulatory gaps might lie to address a public health challenge that is inherently transnational. Several single-country studies acknowledge regulatory shortfalls (Erhun *et al.* 2001; Krech *et al.* 2014), but none of the reviewed papers provide an in-depth analysis of these regulatory challenges. Additionally, the few single-country studies that partly analyse policy responses to reduce the circulation of poor-quality medicines, do not do so from a social sciences perspective (Krech et al. 2014; Erhun et al. 2001; Moken 2003; Abdoulaye et al. 2006; Rudolf & Bernstein 2004). More empirical research from a social sciences perspective is required to explain policy developments against the challenges posed by poor-quality medicines.

3.4.3   Comparing frames and policy processes across borders

Authors concur that cross-sectoral and cross-border coordination is essential to addressing a cross-border phenomenon exacerbated by trade liberalization (Bigdeli *et al.* 2012; Gastrow 2013; Yao 2006; Dégardin *et al.* 2014; Newton *et al.* 2014; Seear 2013). Regardless, none of the studies reviewed in this chapter offer comparative observations of how the problem is understood across countries. More empirical research is required to compare variations in how this policy issue is understood among policy actors. Further investigation is also required on policy developments across national settings and to explain the challenges and opportunities for more systematic policy coordination across countries. Christian and colleagues (2012) provide a brief overview of regulatory challenges in six LMICs and emerging economies; however, none of the studies reviewed offer an in-depth comparative multi-country analysis of frames and policy processes. More specifically, there has not yet been a comparative analysis of frames and policy processes in a regional context where cross-border circulation of poor-quality medicines is an immediate challenge. This supports the choice of case study for this thesis, in which I compare understandings of the policy problem and the development of a policy response to poor-quality medicines in three countries that share borders and belong to a common regional construct – the GMS.

3.4.4   In context: poor-quality medicines in LMICs

Few of the studies reviewed explore the problem of poor-quality medicines in LMICs. Results suggest a lack of empirical research on the problem of poor-quality medicines in LMIC settings. Authors do note the asymmetrical impact of the poor-quality drug trade on LMICs

vs. HICs, arguing that it perpetuates the cycle of poverty in resource-poor settings, due to higher rates of illiteracy or to general information asymmetries (Christian *et al.* 2012; Khan, Okumura, *et al.* 2011; Sipahi *et al.* 2014; DeKieffer 2006; Karunamoorthi 2014; Ahmed 2013; Bird 2007). Despite these insights, the studies reviewed provide little understanding as to whether the drivers and determinants summarized in this review are valid across LMIC settings, and how these might vary depending on their level of infrastructure and economic status. Further empirical research on the problem of poor-quality medicines in different LMICs and how the problem is perceived in these settings, could enhance our understanding of this asymmetrical impact. Interestingly, the literature discusses the relation between the high price of authentic medicines, the attraction it creates for counterfeiters in view of high profit margins (Chika *et al.* 2011), and the demand this engenders for cheaper alternatives in LMICs (Kelesidis & Falagas 2015). However, few authors discuss the reasons why essential medicines available for free or at a subsidized price in LMIC health facilities or generic medicines, are also at risk of being falsified. More empirical research is required to understand these links, and, to do so, this thesis explores the case of antimalarial medicines (AMLs) in three specific national contexts: Cambodia, Laos and Thailand.

Chapter 4   Analytical Framework

In this first section, I detail how the themes that emerged from the literature review and the conceptual framework introduced in Chapter 3, inform the analytical approach employed in this study. Empirical research allows for the exploration of policy actors' interpretations of policy issues across national contexts. In this thesis, I adopt a framing analysis approach to depict actors' interpretations of the policy problem of poor-quality medicines, their understanding of its determinants and how these may shape policy outcomes. Framing analysis facilitates a process of interpretation of policy actors' perceptions and explores the cognitive basis for policy decisions and actions (Druckman 2004). Studying frames helps the researcher in social sciences and health policy understand and explain the underlying role of ideas in refocusing the debate on a policy issue and subsequently in shaping the response to that issue (Medrano 2003).

I start with an introduction on the role of 'ideas' in shaping interpretations of policy problems and in shaping policy responses. I then define what is meant by 'frame' and introduce the framing analysis approach. Subsequently, I explore the interpretation of frames within a policy context, the role of policy actors in the promotion of one frame over another, and how certain frames are more salient than others. Finally, I explain the value of conducting a comparative study highlighting similarities and differences in the use of frames, across policy communities and across national settings, to explain variations in policy developments and the potential for cross-border policy coordination.

4.1   Ideas in policy: the role of frames

Politics itself is a 'struggle of ideas' (Stone 2001, p.11) and the basis of the analytical framework for this thesis rests on the assumption that ideas influence policy making processes. I borrow elements from social constructivism and, in particular, the premise that policy actors' perceptions, policy decisions and their actions are shaped by ideas and social interactions rather than exclusively material interests (Wendt 1999; Ruggie 1998; Klotz & Lynch 1999; Béland & Cox 2011; Gofas & Hay 2010). Craig Parsons (2002, p.48) defines ideas as 'subjective claims about descriptions of the world, causal relationships, or the normative legitimacy of certain actions'.

Social constructivists also argue that policy change is not exclusively driven by a top-down decision-making approach but instead by a dynamic exchange of ideas, extending the analysis of the role of ideas beyond the state-centric approach. It is the ideas of a variety of policy

actors, with influence on the policy process but not necessarily with executive decision-making power that shape policy processes, rather than the ideas of policy *makers* alone. For example, non-government policy actors that work closely with policy makers are part of a policy community whose ideas may also influence the policy making process. Constructivists within the discipline of International Relations add that ideas are inherently dynamic and in constant evolution (Finnemore & Sikkink 1998; Wunderlich 2013), leading to continuous policy change. The dynamic and context-dependent nature of ideas means that they not only vary across time, but also between policy communities and across national settings (Wendt 1987; Ruggie 1998). This study therefore explores interpretations of the policy problem of poor-quality medicines among policy actors, within different institutions and across countries.

Considering the importance of the role of ideas in policy making, I adopt an interpretive approach to framing and policy analysis, one which focuses on analysing policy actors' ideas or varying interpretations of policy problems and policy solutions as influenced by their values, beliefs and experiences (Yanow 1996; Fischer & Forester 1993; Fischer & Gottweis 2012). I examine the ideas on which policy actors' understanding of the policy issue of poor-quality medicines are based, and analyse how these ideas are subsequently communicated within the policy realm (Fischer 2003; Yanow 1996).

4.1.1 Frames as policy ideas

The concept of frames was initially developed in the field of sociology by Erving Goffman (1974). The principal claim of this approach is that any interpretation of a social situation is built on actors' experiences or, in other words, their subjective interpretation of events (Goffman 1974). A frame is a device used to convey a specific idea or understanding of an issue or event; it is an expression of both an actor's interests and identity (Payne 2001, p.39; Barnett 1999, p.25). It is therefore a way of interpreting information and making sense of a complex reality (Entman 1993) and a way of 'packaging and positioning an issue so that it conveys a certain meaning' to a policy problem (Menashe & Siegel 1998, p.310).

Frames are formed along pre-established sets of values and cultural concepts, also referred to as core principles (Fischer 2003; Iyengar 1991; Parkhurst 2012) or as 'ideational paradigms' (Rushton & Williams 2012). As Kathryn Sikkink argues, frames should be interpreted as part of an ideational context shaped by history: 'new ideas do not enter an ideological vacuum. They are inserted into a political space already occupied by historically formed ideologies' (Sikkink 1991, p.2). Frames may, for example, rest on wider global norms, such as the human rights norms. A norm may act as the core principle influencing policy actors' interpretations

of reality, which in turn influence the policy process. The international norm against racial discrimination, for example, encouraged policy actors within the African National Congress to frame their interpretation of events in a segregated South Africa in the 1980s with the aim of advocating against apartheid (Klotz 1995). Payne (2001, p.39) explicitly draws the link between frames and norms arguing that frames are the 'building blocks' that promote the adoption or rejection of a norm. Norms are in turn reinforced by shared conceptions of a problem in line with policy actors' beliefs and cultural preconceptions (Finnemore & Sikkink 1998, p.894). Actors' interpretations of a policy problem, therefore, can be seen as 'cognitive frames' (Finnemore & Sikkink 1998, p.897) built around a norm or a core principle, as well as on the experiences of a policy actor.

4.1.2   Framing as a policy act

Framing is the act of applying, reviewing, contesting, or aligning varying subjective interpretations of a problem in a dynamic fashion (van Hulst & Yanow 2016). Frames essentially set the parameters of a public policy debate (Nixon et al. 2015). The process of framing affects policy development in that it prioritises one interpretation of a policy issue over another. For example, actors may attribute blame or responsibly for the issue in a selective way, and therefore advocate for particular solutions to the policy problem (Iyengar 1991; Stone 1989). The act of framing therefore cannot be dissociated from *politics* and framing is essentially a 'political act' (Hawkins & Holden 2013). Schön & Rein (1994, p.23) explain that frames are 'structures of belief, perception and appreciation that underline policy positions', highlighting the link between framing and policy development. Gusfield (1991) and Jasanoff (2005) explain how the problem of road accidents was re-framed in the United States in the 1970s, leading to policy change. Road accidents were re-framed as a problem linked to drunk driving, prompting policy reforms to penalise drunk driving, alongside policies requiring obligatory use of seatbelts. *Framing analysis* therefore can provide insights into how stakeholders conceptualize a policy problem, and how their interpretations of the problem influences political will and subsequently shapes policy response.

4.1.3   Frames in global health policy

As demonstrated in their literature review of framing studies in public health literature, Koon and colleagues (2016) re-iterate that while frames do influence policy, few studies have analysed the influence of framing on *health* policy processes, especially in low and middle income countries (LMICs) (Koon *et al.* 2016; Parkhurst 2012). Framing analysis is useful to gain a better understanding of complex challenges in policy making, including in global health

policy (McInnes & Lee 2012a). For example, previous studies have explored the use of particular frames to interpret and define global health policy issues, such as pandemic influenza, HIV/AIDS or antimicrobial resistance (McInnes et al. 2012; Kamradt-Scott & McInnes 2012; Woodling et al. 2012; Reubi 2012). McInnes & Lee (2012) introduce these global health frames, all of which are applied to different global health policy issues, in subsequent articles of the same *Global Public Health* volume (Woodling et al. 2012; Rushton 2012; Kamradt-Scott & McInnes 2012; Reubi 2012; McInnes et al. 2012; Williams 2012). Authors of this volume introduced the evidence-based medicine frame, the economics, development, human rights, and the security frames.

The evidence-based medicine frame has been widely used in health policy to justify policy change, as medical decisions and quantitative data (such as mortality and morbidity rates) are seen as 'neutral' and more trustworthy (Parkhurst 2012). Another example is the emergence of global health security as a concept, and subsequently as a frame for infectious disease threats such as H1N1, H5N1 and SARS, which has served to gather financial and human resources, and to encourage cross-border coordination to tackle infectious disease pandemics. Framing the problem of antimicrobial resistance (AMR) in terms of global health security, for example, may raise the issue to the highest political agenda and encourage cross-border cooperation. While framing AMR solely as a medical issue, with an emphasis on clinical evidence, may fail to harness political will for a coordinated response and to allocate resources to improving the rational use of antimicrobials within borders. Frames in global health have served to alter what communities perceive as a risk to national or international health. As another example, HIV/AIDS has been successfully framed as a global health priority, raising the importance of a coordinated response to HIV/AIDS on the global health agenda. This resulted in over a third of all major international funding for health in the 2000s being directed towards efforts against HIV/AIDS, despite the fact that the disease only accounted for around 5% of worldwide mortality and morbidity (Shiffman 2009; Lopez et al. 2006). Keeping an issue on the agenda can be crucial, for example in the case of malaria, to counter dwindling financial and human resources directed towards the disease and to ensure continuous support for efforts towards malaria elimination, and to prevent resurgence in the areas in which the disease is still endemic or where drug-resistant malaria is a concern.

In this study, I refer to six global health frames used to discuss the health policy problem of poor-quality medicines, as summarised below (see Table 3 page 65). This list of frames was initially developed to reflect the themes that emerged from the literature review on the debate around the problem of poor-quality medicines, and refined according to the previously

identified global health frames in literature on framing analysis in global health policy (McInnes & Lee 2012a). It was then adjusted iteratively, during the analysis of the data collected. The frames listed are discernible from the accounts of all policy actors interviewed for this thesis.

I refer to the evidence-based medicine frame as the medical frame in this research. I use the security frame as introduced in the literature on global health frames. I combine the economic and development frames to encompass all economic determinants of the trade in poor-quality medicines in LMICs: from issues of demand and supply to the price of medicines and the challenge of poverty. As we have seen in Chapter 3, the political context was deemed an important determinant of the trade in poor-quality medicines, as well as the legal and regulatory capacity of nations to monitor pharmaceutical supply chains. Issues relating to laws and policy frameworks are encompassed under the regulatory frame, while issues of vested interests, political power struggles or lack of transparency are encompassed under the political frame. As noted in the conceptual framework, issues around access to medicines as a component of the right to health are analysed in the wider context of health systems to reflect on the health infrastructure and the provision of health services and commodities in a given context. In this study, I use the health systems frame which encompasses components of the human rights frame as proposed in the literature on global health frames. This categorisation was decided iteratively based on observations from the data. None of the respondents interviewed framed the problem of poor-quality medicines as a human rights concern per se. There were no explicit references to human rights law or to the right to health during the interviews. Instead, respondents referred to challenges to access to medicines for vulnerable populations with respect to broader health systems constraints – including poor health infrastructure and service delivery and poor accessibility to health services and health products in remote and rural areas. While acknowledging the problem of access to medicines under the health systems frame, the human rights frame specifically did not emerge from the results of this study. This finding is not entirely surprising as the right to health has been gradually understood as "strengthening health systems", and in return, the "building blocks" to a functioning health system relate to the determinants of health that are necessary to achieving the highest attainable standard of health (Hunt & Backman 2008). For this reason, the 'health systems frame' in this study encompasses components that have been included under a human rights frame in previous framing analysis studies, including accessibility to services and commodities for all. I also note here that the socio-cultural determinants of the problem of poor-quality medicines was not a dominant frame in policy actors' response and as such is not

included in this list. However, socio-cultural practices, beliefs and behaviours were considered throughout data analysis.

Frame	Description
Medical	References to evidence-based medicine or evidence of disease burden as influencing policy decisions; bio-medical data to highlight the danger to the health of patients, or other quantitative data such as prevalence rates, etc. This frame has been previously used to inform policy responses against the influenza epidemic (Kamradt-Scott 2012) and by anti-tobacco activists to promote tobacco control policies (Reubi 2012). In relation to poor-quality medicines, this frame encompasses issues around drug efficacy, drug resistance and the medical consequences of using drugs of susbtandard quality.
Security	References to the integrity of the state and protection of populations. This frame has been used to raise pandemic influenza on the global policy agenda (Kamradt-Scott & McInnes 2012) or to define HIV/AIDS (Rushton 2012) as a security threat, encouraging the cross-border coordination of policy responses. In relation to poor-quality medicines, this frame refers to the threat to national security, concerns for the territorial integrity and matieral interests of the state, or to the threat to the wellbeing of a population. It also encompasses references to regional or global security threat; a phenomenon that extends beyond national borders.
Economic	References to trade interests and globalisation, as well as the impact on economic development. The economic frame is also used in the promotion of tobacco control policies to highlight the economic costs of smoking for the nation (Reubi 2012). In relation to poor-quality medicines, this frame encompasses issues around demand and supply, the lucrative nature of drug falsification as an activity. It is considered a dominant frame in the debate around the protection of intellectual property rights and patenting in support of drug development.
Health Systems	References to the health infrastructure, the organisation of people and resources to deliver health services and commodities to meet the population's health needs. The health systems frame for this thesis encompasses principles of equity and universal health coverage for all. In relation to the problem of poor-quality, this frame encompasses the ATM debate around making affordable, generic medicines more widely available to improve access to quality medicines for all. It also encompasses issues around the procurement and distribution of medicines (Bigdeli *et al.* 2012; Frost & Reich 2008).
Political	References to political culture, corruption or vested interests – all of which can have a negative impact on the implementation and

	enforcement of rules and regulations and lead to the inequitable distribution of resources (Mackey & Liang 2012).
	In relation to poor-quality medicines, this frame encompasses cases of vested interests from government officials in the production and distribution of substandard or falsified medicines. It can also refer to the untransparent management of procurement funds or of politically-sensitive data on poor-quality medicines.
Regulatory	References to laws, policies and governance mechanisms in place to address health policy issues.
	In relation to poor-quality medicines, this frame encompasses the status of national medicine regulatory frameworks and how adapted these are to a complex, trans-border nature of this health policy problem. This frame also encompasses government's capacity and capability to regulate in terms of the resources available to implement and enforce laws and policies (Attaran 2015b; Bate et al. 2012; Nayyar et al. 2015).

Table 3 Description of the six health policy frames used in this study

More than one of these frames can apply to the same global health issue (McInnes & Lee 2012). In this thesis, I analyse policy actors' perception of the health policy problem posed by poor-quality medicines in the national and regional context of the GMS. I juxtapose their responses against the six frames summarised above and evaluate which ones are more dominant across national settings and across categories of respondents. A systematic analysis of these six frames across three national settings allows for the comparison of variations in how the policy problem is interpreted across national settings, and what the implications of these variations are for cross-border policy coordination.

4.1.4   What makes a frame successful

Some frames are more salient than others – they resonate better with policy actors and shape policy responses, with a higher success at placing a given health policy issue on the agenda. McInnes & Lee (2012) propose the following criteria for evaluating the success of a frame: they assert that firstly, the power and authority of the policy actor is what makes one frame dominant over another (Shiffman & Smith 2007; Rushton 2012; McInnes & Lee 2012a). Rushton (2012) highlights the pivotal role of civil society organisations in the global debate over HIV-related travel restrictions. The power and authority of a policy actor depends on his or her position within policy communities, the notoriety of the individual, or the strength of the guiding institution in which he or she operates (Shiffman & Smith 2007). The second element is the ability for a frame to draw on the material world (McInnes & Lee 2012a); to refer to events and specific developments in the global realm or in society (for example, the Ebola Virus epidemic). The third element relates to the (socio economic or political) context

in which a frame is introduced and how receptive an audience is to that frame (McInnes & Lee 2012a). McInnes & Lee (2012) refer to a study by Kamradt-Scott & McInnes (2012), which argues that the security frame around pandemic influenza was only successful after the end of the cold war, when the political audience became less concerned with security matters related to nuclear proliferation and more receptive to the problem the health threat of influenza. Shiffman & Smith (2007a) add that the nature of political contexts in which a frame is promoted matters, that is, the governance structure of the political environment and the opportunities for policy change that develop in favour or against a frame.

McInnes & Lee (2012) add that a frame is sometimes only successful after a 'tipping point' leading to its acceptance. They cite Rushton (2012), whose study of travel-restrictions on HIV positive individuals suggests that the change of policy in the US against these travel restrictions was a tipping point to convince other nations of the validity of the human rights frame advocating against these restrictions. Finally, a frame only becomes dominant if it is able to adapt to changing contexts over time (McInnes & Lee 2012a). A flexible frame can draw on multiple material events and to leverage different audiences at once.

Beyond the criteria of a successful frame proposed by McInnes and Lee, Menashe & Siegel (1998) explain that frames becomes dominant when they rest on core principles that resonate well among policy communities such as fairness, equity, autonomy, freedom or the protection of human rights. Additionally, a frame may be successful because of the issue characteristics of the problem it presents; either the severity of the problem, or the plausibility of the policy solutions proposed in this frame (Shiffman & Smith 2007). Shiffman (2009) encourages a more systematic use of framing analysis to understand why certain interpretations of a policy problem prevail over others. For this reason, I conduct an analysis of frames used by policy actors on the problem of poor-quality medicines, with the help of a dynamic model of policy analysis, as will be introduced in the following section (4.2) of this chapter. The success of one problem definition over another therefore depends on all the elements introduced above. These elements are explored throughout this chapter when reflecting on the role of policy actors (section 4.2.2), on the policy context (section 4.2.3), and on processes of frame alignment (section 4.2.4).

4.2   Framing analysis and policy development

In this thesis, I analyse variations of frames used by policy actors and their implications for policy development. I adopt an interpretive policy analysis approach which focuses on 'the construction of social reality and the symbolic use of language within policy debates'

(Hawkins & Holden 2013; Edelman 1988). This entails a reflection on how frames shape policy processes (Hawkins & Holden 2013) and necessitates a preliminary understanding of the policy context in which these frames are being promoted. Sabatier and Jenkins-Smith (1993) introduce three stages to guide policy analysis, from problem identification, to policy formulation and, subsequently, policy implementation. The stages approach is useful as a heuristic tool to guide the analytical process along the phases of policy making. However, the policy process is better described as cyclical rather than linear (Fischer *et al.* 2007) and as a dynamic process where the problem *definition* becomes part of the policy *solution*, and the outcome of policy implementation will subsequently contribute to the redefinition of that problem, feeding back in the policy cycle in a continuous loop (Parsons 1995).

In this thesis, I study the processes through which 'frames emerge and are maintained' (Hawkins and Holden 2003) or in other words, the process of issue formation. The policy process is understood here as 'the way in which policies are initiated, developed or formulated, negotiated, communicated, implemented and evaluated' (Buse *et al.* 2005, p.4). For this thesis, I borrow elements from the policy triangle model (Walt & Gilson 1994) and the multiple streams model (Kingdon 1984; Kingdon 1995) to reflect on the role of framing in policy making. Throughout the analysis of frames, I reflect on the policy process around the goal of improving access to quality medicines. Weible *et al.* (2012, p.3) explain that studying the policy process involves studying 'the development of public policy over time and the context, events and individuals surrounding this development'. I therefore reflect on four elements of the policy process introduced by Walt & Gilson (1994), namely: the content of the policy problem; the role of actors; the policy context; and the policy process – as outlined in the diagram below. The multiple streams model (Kingdon 1984; Kingdon 1995) provides further insights into how a particular policy issue reaches the policy agenda and focuses specifically on policy issue formation and definition. This model helps us understand how policy issues come to the attention of policy actors (Kingdon 1984). It consists of three main streams – the problem, the politics and the policy stream – which contribute to shaping the definition of a policy issue and its perceived policy solutions.
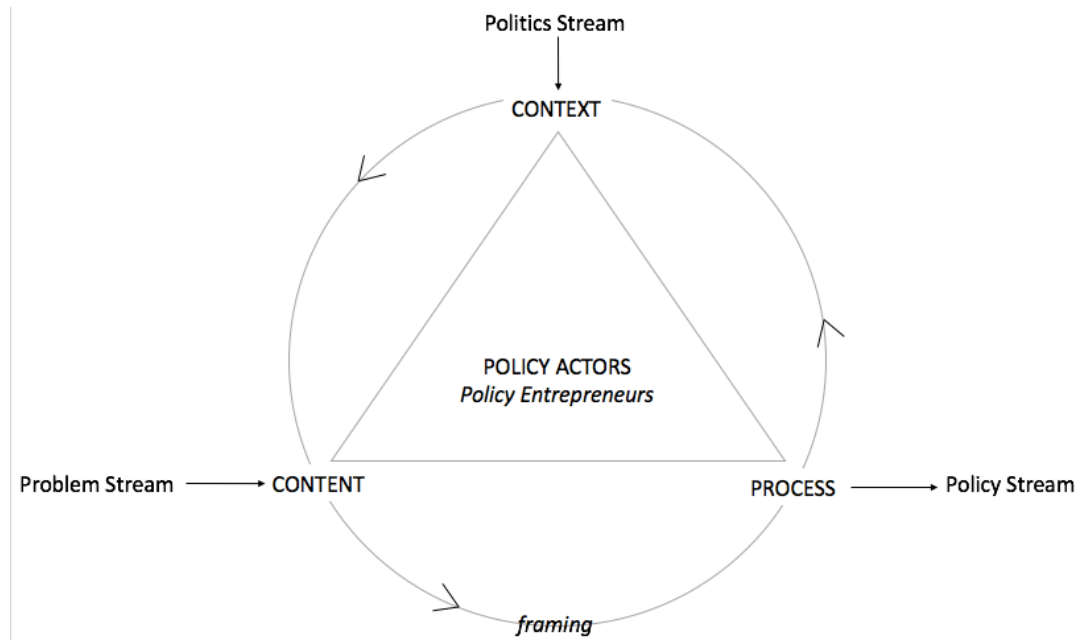
Figure 5 Combined frameworks for framing analysis in policy context

The proposed combined analytical framework encouraged a more dynamic interpretation of the role of policy 'actors' at the centre of this model, with the iterative process of framing and reframing of the policy problem. It also encouraged a more careful awareness of the 'context' in which this policy problem is interpreted. It guided the analysis of frames within a dynamic policy process and facilitated the systematic analysis of empirical data on policy actors' perceptions of the problem of poor-quality medicines in three national contexts, thereafter allowing a comparison of the results across these national settings. This section details the application of this model to the study of frames.

4.2.1   Framing and problem definition

In an introduction to the policy cycle, Parsons (1995 p. 88) argues that the 'definition of the problem is part of the problem', that perceptions and constructions of policy issues are important at all stages of the policy process. Delineating the content of a policy problem requires an understanding of actors' perceptions of this problem, their stories around it, the themes they refer to and the meaning that they attribute to the policy problem (Fischer 2003). In this thesis, I analyse how the problem of poor-quality medicines is problematized by policy actors. Analysing policy frames is one way to study interpretations of a policy problem (Schön & Rein 1994). These interpretations may vary from one policy group to another, and it is relevant to study the competition for attention between different frames across institutional settings. Framing analysis therefore helped me understand 'what is going on' and what aspect

of a policy issue is considered a problem requiring a policy response (Goffman 1974; Koon *et al.* 2016). Through the analysis of frames, I explore the key determinants, indicators or 'focusing events' that shape the perceptions of this policy problem among key policy actors. 'Focusing events' can be understood as global or national events that generate public interest and trigger policy shifts, e.g., a financial crisis, natural disaster, terrorist attack, or an epidemic (Kingdon 1995).

The way that a policy issue is defined influences the policy agenda[27], i.e., framing influences what themes become foci of attention and which policies take priority over others (Rushton & Williams 2012). Issues that reach the policy agenda shape the development of policy solutions (Fischer *et al.* 2007). Framing a health phenomenon as a security concern[28], for example, could work to raise attention towards this issue by classifying it as a matter of 'high politics', taking prime position on the national policy agenda (Labonté & Gagnon 2010). Different frames shape the policy process by generating variations in 'pathways of response' (Entman 1993; McInnes & Lee 2012a). Framing has also been used to keep health issues on the policy agenda; as demonstrated with the cases of HIV/AIDS. In this thesis, I analyse variations in problem definition and whether and how the problem of poor-quality medicines reaches the policy agenda.

4.2.2   The role of policy actors

Policy actors are understood here as actors with an influence on the policy process, be they government-level actors, civil society representatives, private sector representatives, or even international institutions (Buse *et al.* 2005). In this thesis, I explore the role of two categories of policy actors, namely government policy actors and non-government policy actors, and their varying interpretations of the problem of poor-quality medicines in three national settings. It is through policy actors' interpretations of a policy problem and how the issue is framed and reframed and through their interactions, that policy pathways may change. Policy actors are policy entrepreneurs in that their actions, decisions and interactions influence the policy debate (Kingdon 1995). They promote ideas by investing time and effort at endorsing those ideas in political debate and promoting their uptake on the political agenda (Guldbrandsson & Fossum 2009; Kingdon 1995). Policy actors promote certain frames over others by communicating meaning to a policy issue (Schön & Rein 1994; Edelman 1988). Among constructivists, policy

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[27] The policy agenda is understood as 'the list of subjects or problems to which government officials, and people outside of government closely associated with those officials, are paying some serious attention to at any given time' (Kingdon 1995, p.3).

[28] Also referred to as a process of 'securitization' (Kamradt-Scott & McInnes 2012).

actors are seen as agents of policy change through the construction of 'cognitive frames' around a policy problem or around a policy solution (Finnemore & Sikkink 1998, p.897). The act of framing by policy actors influences which topics reach the policy agenda, therefore shaping pathways of policy response.

4.2.2.1 Issue formation

Policy actors play an active part in a process of issue formation by steering a policy debate. Firstly, policy actors' participation in the process of issue formation goes hand in hand with interest construction. In framing analysis, the main premise is that actors' frames 'determine what they see as being in their interests and, therefore, what interests they perceive as conflict' (Schön & Rein 1994, p.29). Actors' interests in this regard can be both material and ideational, and it is the interplay of both the material and ideational that influences policy actions (Fischer 2003). Sheri Berman (2001) adds that frames can shape both political behaviour (by shaping policy actors' interests) or shape the environment in which policy actors operate. In the latter case, a frame may exert influence on policy decisions because of the consequences of not taking this frame into account. This may occur when a global norm (such as the norm against apartheid) alters the wider political environment, in this case influencing South Africa's decision to reform its policies on segregation.

I argue here that rationality cannot be considered as the only driving force behind policy decision making, as it does not account for the interplay of policy controversies, the competition between interests and ideas, that are inherent in policy debate and in policy development. Habermas (1985), in his introduction of the theory of 'communicative rationality' suggests that actors' policy decisions are anchored in interpersonal constructions of meaning. Wendt, a social constructivist, supports a similar notion, arguing that both ideational and material concepts are not mutually exclusive: 'material forces are not constituted solely by social meanings, and social meanings are not immune to material effects' (Wendt 1999, p.2). Gofas & Hay (2010) further argue that policy researchers should overcome the dualism in modes of inquiry between the material and ideational reality. They explain that 'ideas guide actors towards strategies for attaining their goals and realising their interests' (Gofas & Hay 2010, p.23). Frames and interest formation therefore influence policy action: 'not ideas, but material and ideal interests directly govern men's conduct […] "world images" that have been created by "ideas" have determined the tracks along which action has been pushed by the dynamic of interest' (Weber 1947, p.280). Interest formation is a crucial element of analysis in studying the role of actors in shaping the policy process.

4.2.2.2 Framing and power

Policy actors' power to influence the policy debate depends on their level of authority and the success of their bargaining acts within a policy community. Policy actors who propose and promote these frames essentially make ideas evolve into policies, programmes of action or laws through mechanisms of agency. They do so by organizing information to create meaning, telling policy makers what information is deemed important and how thereafter it influences policy decisions (Mejia *et al.* 2014). Framing is a dynamic act of communication used to justify an interpretation of a policy problem which involves crafting and frames, a means to exert influence and lead policy communities towards a specific course of action. This is a process of frame manipulation whereby policy actors adapt their idea to the local policy context (Payne 2001; Wiener & Puetter 2009). As seen previously, various factors influence the strength of a frame including: *who* is proposing the frame, which matters above all; the level of authority of the frame sponsor or the level of decision making power; as well as the actor's legitimacy and expertise on the policy issue (Rushton & Williams 2012). Power in this sense is exercised through the spread of knowledge and values (Foucault 1980). Power can be measured in terms of resources (such as financial resources, membership and popular support or infrastructure), as well as intangible resources (such as expertise, legitimacy and access to decision makers) (Buse *et al.* 2005). Stephen Lukes (1974) conceptualizes 'power as thought control' in the sense that the power-holder can convince someone to do something that is not necessarily in his/her interest. In framing analysis, power takes the form of blocking or promoting certain policy interpretations and policy solutions over others by re-interpreting a policy problem. It is an essential component to understanding the role of framing in influencing policy developments.

4.2.2.3 Actor interactions

Exploring the role of policy actors and their power to influence the uptake of a frame also means observing the *interactions* between those actors. More than one actor influences policy processes, while not all will have the same understanding of the policy issue (Parsons 1995). Constructivists argue that social constructions of reality are inter-subjective and depend on a shared and common understanding of a phenomenon (Adler 1997; Finnemore 1996). Policy change occurs through interactions between actors and policy subsystems including policy communities, interest and expert groups, and groups of actors gathering around the same policy issue or strategic policy agenda (Marsh 1998). Looking at interactions between policy actors encourages us to analyse both agents and structures jointly (Wendt 1987; Marsh 1998).

Policy actors interact among each other and, in doing so, deliberate and contribute to the spread of information through expertise, resources and power. This crafting process determines the implications of a given frame on policy developments (Sabatier & Weible 2014; Dowding 1995). Institutions are also relevant in that they accompany the development of frames and act as arenas for policy interaction. The President's Emergency Plan for AIDS Relief (PEPFAR) or the Global Fund, for example, are relevant institutions for the mobilization of resources (both human and financial) against HIV/AIDS, and actively support the implementation of programmes and research initiatives in line with the idea that HIV/AIDS remains a global health priority (Shiffman 2009). Changes in the structure of the policy arena (the networks and the policy communities) affect the way that frames influence policy developments. For example, the active involvement of private sector networks representing the innovator pharmaceutical industry may impact policy processes to improve access to affordable medicines, due to a more likely emphasis on the intellectual property frame. Reflecting on the interactions among policy actors, therefore, helps us understand the salience of ideas or frames and the implications of these for policy pathways (Béland 2009; Béland 2010).

4.2.3   Framing in policy context

Analysing frames and the influence of frames on policy developments is highly-context-dependent (Wiener 2012). The analysis of frames is only possible with a thorough understanding of the wider political context in which frames are advanced and policy processes take place. Frames do not do the job at leading policy change alone, but they should be observed as part of a wider political context offering 'policy windows'. A policy window represents an opportunity to 'facilitate policy change' (Guldbrandsson & Fossum 2009, p.435) triggered by a policy reform, or a change in the configuration of domestic politics for example (i.e., a focusing event). For example, international aid funding to support access to anti-retroviral treatments against HIV/AIDS provides a favourable context in recipient nations for frames aimed at prioritising the fight against HIV/AIDS, through strengthening the health system and the distribution supply chain of anti-retrovirals (Shiffman 2009; Woodling *et al.* 2012; Hammonds & Ooms 2014). HIV/AIDS may become a lesser priority if more pressing security concerns affect a nation – such as war or famine. The researcher is therefore encouraged to take into consideration the national mood in which policy decisions are made.

Roggeband and colleagues (2014, p.225) argue that the process of issue formation is about '[negotiating] frames that are better adapted to context specific concerns and that build on regionally emerging commitments, legal frameworks and/or other traditions'. The policy

context also refers to the systemic factors such as economic, geographic, social, and cultural factors specific to the country under study that might influence the policy process. These systemic factors can be observed both at the national and international level. Applied to the study of poor-quality medicines, the policy 'context' encompasses the socio-cultural and economic determinants and drivers of the problem of poor-quality medicines, as summarised in the themes that emerge from the review of literature in Chapter 3.

Leichter (1979) in his study of health policy in four different nations, offers a classification of factors (albeit a very broad classification) that shape a policy context: namely, structural, situational, cultural, and international factors (see also Buse & Mays 2012). Under situational factors, key focusing events such as the seizure of fake medicines, the discovery of malaria-resistant strains, or a global conference on the global threat of pandemic influenza, are likely to influence the policy process at a given point in time. Structural factors include the state of the economy, the political culture and system of a given country, or even its geographical and demographic features – all of which can impact the policy process. Cultural factors include the role of religion, education or illiteracy rates, and the presence of ethnic minorities or evidence of population trust in the political system. Leichter (1979) notes that international factors, including cross border phenomena such as migratory flows or the trafficking of illicit products, but also donor funding, are likely to influence national policy processes. For this reason, it is relevant not only to acknowledge the regional context within which a policy process takes place, but also to compare the policy contexts of more than one case study, to gauge the influence of frames on policy processes in different settings.

4.2.4   Framing solutions and alternatives

The analysis of frames also calls for reflection on the process of framing, re-framing, frame competition and frame alignment – or the process of negotiation among policy actors and between different interpretations of a policy problem. Reflecting on this process allows for an analysis of the implications of framing on policy pathways, the presentation of policy solutions and alternatives. Ideas promoted by policy actors act as 'road maps' for policy development (Goldstein & Keohane 1993; Berman 2001, p.235). Policy pathways are debated in line with specific definitions of the policy content, the policy context and according to policy windows that offer opportunities for policy actors to promote one policy solution over another.

4.2.4.1   Re-framing

In this thesis, I reflect on processes of framing and re-framing, and the implications of variations in interpretations of the policy problem for policy outcomes. As Hawkins & Holden (2013, p.54) explain, frames are used to 'open up certain policy responses whilst precluding others'. The process of framing and re-framing involves a change in narratives by which local stakeholders choose to define the problem and in turn generate or encourage particular patterns of behaviour (Stone 1989). As an example, one country's re-framing of travel restrictions against people living with HIV/AIDS as a human rights infringement, as opposed to a necessary restriction for national security, may influence reforms in other nations that still impose such bans, triggering reforms aimed at removing such restrictions (Rushton 2012). This is an example of a positive outcome of cross-border re-framing. In this study, I observe how the policy problem of poor-quality medicines is framed or re-framed in the three case countries and I reflect on implications of this for policy developments aimed at improving access to quality medicines.

Rein & Schön (1996, p.89) point out that there are two types of frames to explore – the rhetorical and the action frames – both of which influence policy decisions. Rhetorical frames form part of the political debate, often used verbally within policy communities, and aimed at convincing other policy actors of a specific angle and policy solution. Action frames, also referred to as prognostic (vs. diagnostic) frames (Gregorio *et al.* 2010), are articulations of concrete policy strategies, sometimes expressed through policy documents, laws or declarations. In this study, I explore both rhetorical and action frames. This continuous process of reframing, either through action or rhetorical frames, can take many forms including: *frame blending,* when discussions on particular topic are obscured by introducing a complex amalgam of additional frames or themes; *frame shift*, when the use of language steers away from one topic to another; *frame bridging*, when discussions on a topic allude to a different theme altogether; and finally *frame alignment*, when frames construct a meaning around a policy issue that is congruent with local ideas (Snow *et al.* 1986; Mah *et al.* 2014; Rein & Schön 1996; Benford & Snow 2000). Schön & Rein (1994) also discuss *frame reflection* as a mechanism by which policy actors themselves become aware of the non-linear negotiations and competition that occur between different frames of a policy problem.

4.2.4.2 Frame competition

Frames compete with one another with the aim of influencing the policy process. While competing frames may advocate for different policy actions (Béland 2010) these can ultimately have the same policy outcome (L'Espérance 2013). Frame competition, also referred to as 'contestation', takes the form of a debate of themes and counter-themes around a policy issue and led by policy actors (Gamson 1992). This can lead to disagreements between policy communities. This framing debate as a dynamic process of contestation does not necessarily occur between two opposing schools of thought but, rather, between policy actors who promote a different web of values to define a problem and its solutions (Menashe & Siegel 1998). It is important to examine processes of frame competition and contestation, something which, as Payne (Payne 2001) points out, constructivist theory has often failed to encompass. Policy actors are engaged in a continuous, sometimes tacit, process of frame competition. This process is the outcome of struggles between different perceptions of reality and 'meanings' attributed to a policy problem (Snow & Benford 1992; Gamson 1992; Yanow 1996) related to a course of action which either solves or ignores this policy problem (Barnett 1999; Risse & Sikkink 1999; Payne 2001) and sometimes leading to policy controversies (Schön & Rein 1994). Understanding the process of frame competition is necessary 'to understand ideational change' and to understand 'the reasons why ideas are discredited, new ideas are advocated by important carriers' while others are not (Berman 2001, p.236). This is only possible through a thorough analysis of the policy process – how ideas are promoted over time and by which actors (Payne 2001). In this study, I reflect on the interplay between salient frames and evidence of frame competition in each national context and between different categories of policy actors.

4.2.4.3 Frame alignment

Frame alignment occurs when a frame is congruent with policy actors' preconceived ideas, values and interests of policy actors and in line with the wider policy context (Béland & Cox 2011). Frame alignment occurs when an interpretation of a policy issue 'resonates' best with the political culture of local policy makers (Gamson 1992; Iyengar 1991) and deeply embedded ideas (Shiffman & Smith 2007; Sabatier & Weible 2014). Kingdon (1995) adds that proposed frames are successful if the policy solutions that the frame entails are judged feasible and if the resources are aligned for its implementation. Frames resonate internally if they unify policy communities around a common definition of a policy problem and they resonate externally, if they successfully move policy actors to action (Shiffman & Smith 2007).

Analysing instances of frame alignment can help understand which frames might lead policy change.

In this study, I reflect on which frames are salient among the policy communities around access to medicines in Cambodia, Laos and Thailand; or, in other words, which frames are repeated and presented as important in the debate on access to quality antimalarial medicines. I reflect on which frames prevail over others and how those might influence policy efforts against poor-quality antimalarial medicines. I observe which combinations of elements in the policy process – be it the actors, networks, the policy context or the nature of the problem definition – contribute to the policy developments against poor-quality antimalarial medicines. In doing so, I analyse instances of frame blending, shifting, bridging, and alignment where relevant. Framing analysis offers a lens through which I can explain the process of political contestation between actors with differing agendas and priorities.

4.3   Logic of comparison

I have introduced the concept of framing, frameworks for policy analysis, and how to explore the impact of frames on policy processes. This section explains the value of comparative analysis to explore variations in perceptions of the problem of poor-quality medicines across three Southeast Asian countries, and subsequently to reflect on the implication of these variations for regional cooperation. I detail the logic of comparison that drives the comparative qualitative analysis of this thesis.

4.3.1   Comparative framing analysis

Comparative qualitative research, Hokin (2010) explains, is well adapted to the study of ideas from a constructivist perspective as it allows the researcher to explore the links between more than one ideational factor and a process in various settings. Comparative analysis in qualitative research, combined with framing analysis, has been applied previously in studies by Juan Diez Medrano (2003) and Sheila Jasanoff (2005). Both authors adopt a comparative approach to study the role of ideas in policy making between three countries. Medrano (2003) explores attitudes among citizens of Germany, Spain and the United Kingdom towards European integration. Jasanoff (2005) explores frames and ideas in biotechnology and life sciences and variations in three different countries: Germany, the United Kingdom, and the United States of America. Both studies are anchored in sociology but draw on elements of constructivism and framing analysis. Neither of these studies, however, offers a comparative approach to framing analysis in low-middle income countries. Nevertheless, the studies by both Medrano

and Jasanoff are a great source of inspiration for my own comparative work in framing analysis around the problem of poor-quality medicines. This thesis differs from their approaches in that it reflects on the implications of variations in framings of a cross-border *health* policy problem for cross-border policy coordination.

The comparative case study approach enables the researcher to contextualise findings through in-depth case studies and, subsequently, to compare the main findings and depict salient concepts or frames across the case countries (Kalleberg 1966). This provides an opportunity to analyse a complex empirical problem in three different settings and to draw generalisations from the combined data (Dogan & Pelassy 1990; Lim 2010; Hargue & Harrop 2007). Such an approach improves the validity of empirical observations. Comparative analysis, therefore, provides an opportunity to understand a complex empirical problem within a wider regional context, and offers a way to interpret and assess findings across institutional and national settings. For my study, the comparative approach provides an opportunity to explore the nature of the problem of poor-quality medicines and how it is framed and addressed in three different settings, and to observe potential for cross-border cooperation for improving access to quality medicines. This approach offers a dynamic application of a theory level analysis (impact of frames on policy processes) and the empirical level (explaining the problem of poor-quality medicines) (Burnham *et al.* 2008).

The three case-countries within the GMS were selected because they are comparable in that they have both important 'shared' and 'non-shared' attributes among them (Sartori 1994). All three case countries share borders within the GMS and are members of the Association of Southeast Asian Nations (ASEAN). The Mekong River flows through each of those countries, they share similar tropical-wet climates and have comparable epidemiological profiles for malaria. On the other hand, the countries selected belong to different income groups[29] and have different political histories and systems. Despite these shared and non-shared attributes, the three cases are all affected by the same policy issue (the problem of poor-quality medicines) – although it is articulated differently in each national context. Combined, these three case countries provide comparative ground to analyse variations in how the problem of poor-quality medicines is framed across borders.

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[29] Lower Middle Income (Laos and Cambodia) to Upper-Middle Income (Thailand),

4.3.2   Comparing frames and policy developments

The dependent variable in comparative research is the phenomenon under study which is common to all cases, while the independent variables are the factors that influence this phenomenon causally (Burnham *et al.* 2008). For this study, the dependent variable is the problem of poor-quality antimalarial medicines, while the frames used to define this phenomenon are the independent variables. While making general observations is useful to highlight trends and to understand common or divergent interpretations of the problem of poor-quality medicines in the GMS, I remain aware of the fact that the data only represents reality as far as the data collected from the three out of six GMS countries or states are concerned.

The comparative approach applies to this thesis in two ways. 1. To set the scene for the analysis of frames, I start with a brief overview of the policy processes for improving access to quality medicines and reducing the circulation of poor-quality medicines in Cambodia, Laos and Thailand. This first step was useful to draw parallels between policy processes and the implications of framings for a policy response. Throughout this process, I acknowledge the similarities and discrepancies in policy across national settings. 2. I then proceeded to compare how the problem of poor-quality medicines is framed in each country, both within its legal and policy documents and among local policy actors; and observe the similarities and differences between interpretations of the problem of poor-quality medicines across institutional settings and between national settings. I base my analysis on a set of six pre-determined frames around the problem of poor-quality medicines. By comparing framings, I depict overlaps and reflect on the dominant frames used in the region to explain the determinants and the challenges linked to the problem of poor-quality medicines. I reflect on variations in how the same frame is articulated within different policy communities and across the three countries.

4.3.3   Cross-border policy coordination

In the discussion chapter for this thesis, I use the findings from my comparative analysis to reflect on the implications for regional policy coordination to address the common problem of poor-quality medicines. As the problem of poor-quality medicines extends beyond national borders, I reflect on whether definitions and interpretations of the problem affects the propensity for Mekong countries to work together to improve access to quality antimalarial medicines. Framing analysis provides the lens through which I reflect on shared ideas, that may be diffused, contested, or internalized within and between countries, and how those might influence responses to this policy challenge (Finnemore 1996; Finnemore & Sikkink 1998; Finnemore 1993; Risse & Sikkink 1999). Ideas transcend national borders through processes

of diffusion (Béland 2010), sometimes via frames promoted across different national settings by international organization such as the World Health Organization. This contributes to knowledge sharing and lesson drawing from policy initiatives between different national settings. Knowledge sharing involves a process of persuasion, whereby actors of a different policy setting acknowledge the relative advantage of a policy from a different time and place, and recognise its compatibility for their setting (Bissel *et al.* 2011).

While discussing the results, I evaluate the potential for lessons to be drawn to enhance policy coherence between the three case countries. I reflect on evidence of strategies, policies, programs or tools adopted and applied in another policy context because of their perceived feasibility, validity and adaptability. Comparing policy processes provides an opportunity to reflect on cross-border knowledge generation and exchange. While variations in frames may imply differences in political culture which in turn may impede collective action, similarities in how an issue is framed may provide ideational grounds for it (McInnes & Lee 2012a).

Shared understandings of the problem of poor-quality medicines between neighbouring countries may also lead to a common regional understanding of a policy issue, facilitating policy transfer and adoption. Exploring how policy actors across national settings interpret the problem of poor-quality medicines and whether their ideas are shared, could explain the presence of 'collective intentionality' for cooperative action (Khagram, Riker, & Sikkink 2002). Policy coherence occurs through knowledge and expertise sharing, and evidence of strategies, policies or programs being adapted and applied to a different policy context (Bissell e*t al.* 2011; Dolowitz & Marsh 2000). Reflecting on policy coherence involves taking into consideration the processes of knowledge sharing, communication and persuasion between policy actors in different national settings, and to reflect on what factors may facilitate policy coordination across borders.

The comparative approach, in which findings are juxtaposed to reflect on the wider, regional context, addresses Galton's problem in comparative research, which notes the importance of studying the impact of external factors on empirical relationships (Burnham *et al.* 2008). In the discussion chapter (9) of this thesis, I raise important questions in line with cross-border cooperation, policy coherence and regional health governance. Results suggest, for example, that ASEAN, as the main supra-national platform for political debate, has a role to play in fostering policy coherence against the threat posed by poor-quality antimalarial medicines. For this reason, it is useful to explore the specific characteristics of cross-border and regional politics; such as differences in political culture, decision making processes and existing

mechanisms for accountability (Acharya 2009; Khagram *et al.* 2002). This comparative approach offers a way to interpret similarities and differences in results across three national settings and to explore the interactions between framings of a policy problem in different policy contexts (Hokin 2010), as well as the implications of variations in framings for cross-border cooperation.

Chapter 5   Methods

The methods of qualitative research outlined in this chapter support the aim of this study, which is to analyse and compare framings of the policy issue of poor-quality medicines among policy actors in Cambodia, Laos and Thailand. Few studies have previously explored perceptions around the problem of poor-quality medicines and few studies on poor-quality medicines are qualitative in their approach (Alfadl, Ibrahim, et al. 2013). Qualitative research is particularly appropriate for this study, which seeks to explore the role of ideas in policy. Qualitative research consists of collecting data that *describes* a phenomenon of the social world and thereby helps construct *explanations* for a phenomenon. It offers the opportunity to analyse the perceptions and behaviours of stakeholders whose actions directly influence the phenomenon itself (Seale *et al.* 2004).

5.1   Three methods of data collection and analysis

In this thesis, I use three methods to analyse the framings around the issue of poor-quality medicines in three countries (Hawkins and Holden 2013): (1) stakeholder mapping (Method A) to identify the key policy actors and institutions involved in policy efforts to address the problem of poor-quality medicines; (2) document analysis (Method B) as a method commonly used in the analysis of policy processes, as well as in the analysis of action frames; and (3) semi-structured interviews (Method C) to uncover the dominant frames used among policy actors to define the policy problem in each country and to obtain information on the policy context. The three methods, used jointly, allow the exploration of the interplay between frames and policy developments. Figure 6 on page 82 illustrates how each method builds upon the analytical framework defined in Chapter 4. In this chapter, I explain how each method supports the analysis of frames of the problem of poor-quality medicines, and the implications of variations in framings cross-border policy coordination. I detail the processes of data collection and data analysis (thematic content analysis and comparative analysis), and how the results are presented in this thesis.
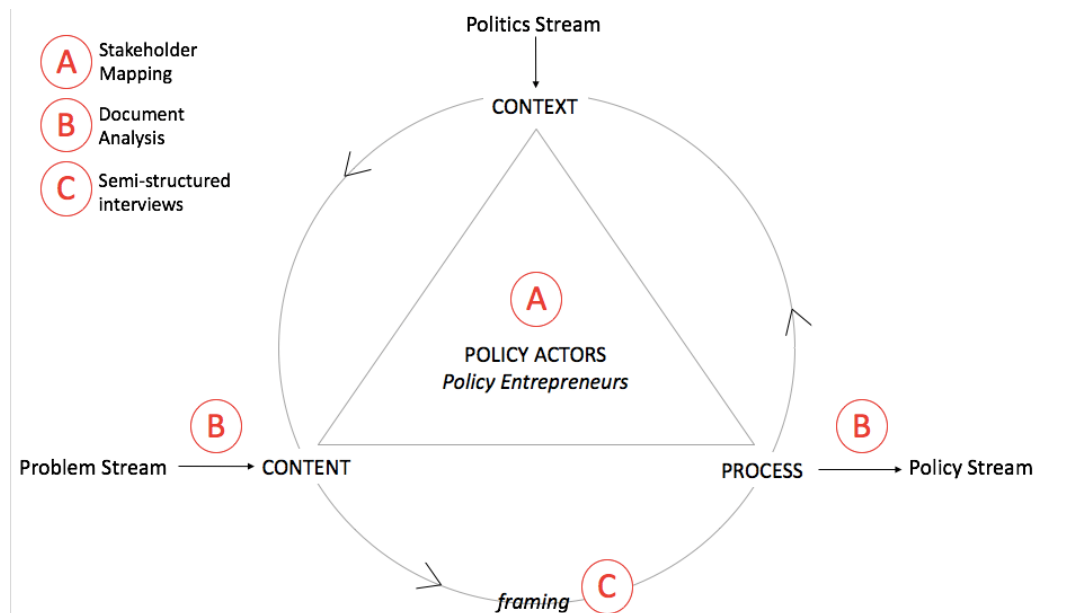
Figure 6 Methods and the analytical framework

The policy triangle developed for health policy analysis by Walt & Gilson (1994) has regularly been applied as a framework to study health policy process around public health issues (Walt *et al.* 2008). The four components (policy actors, content, context and process) of the Policy Triangle have guided both the collection and analysis of data for my thesis, as well as the analysis of the policy processes for each case country. Kingdon's multi streams model focuses on how a policy issue reaches the policy agenda through the intersections of three streams: the problem, politics and policy streams (Kingdon 1984; Kingdon 1995). Both models were useful to analyse how 'frames emerge and are maintained' in three policy contexts (Hawkins & Holden 2013).

5.1.1 Method A Stakeholder Mapping

As a first step in the investigation of the use of frames and policy developments for each country, I identified key policy actors and institutions involved in the policy process through a stakeholder mapping exercise (Method A). This method is placed at the centre of the diagram above, as it informed the rest of the framing analysis process. 'Stakeholders' are understood here as the *policy actors* or institutions whose activities have a direct impact on policy developments (Morgan & Taschereau 1996). As Buse and colleagues (2005) argue, the first stage of analysis of policy processes involves identifying who plays a role in shaping and implementing a policy, and what the interactions between those actors are. Stakeholder mapping is not only a useful tool to identify the key policy actors, but also to map the main

relationships between these actors, the recurring interactions or the key networks for the exchange of information (Ostrom 2009; Aligica 2006). It offers the possibility to evaluate which policy actors have most influence on the policy process, as frame sponsors, policy entrepreneurs or leaders of a policy change. This mapping exercise allowed me to explore notions of power as well as agency, and to reflect on the accountability of stakeholders to each other, in addition to the sustainability of their interactions; or in other words, whether an initiative is locally-led or whether it was part of a donor-dependent and time-restrained initiative spearheaded by an international institution (McGinnis 2011). Mapping stakeholders was a useful tool both for identifying key documents for analysis (Method B) and to identify participants for the semi-structured interviews (Method C). In return, the findings from Methods B and C provided additional information that fed back into this mapping exercise.

5.1.2   Method B Document Analysis

This second method was useful to uncover the official definitions of the problem of poor-quality medicines as stipulated in legal and policy documents, to study policy processes and to inform my analysis of the wider context for each case country. Analysing key policy and legal documents provided an opportunity to explore how the policy issue of poor-quality medicines is defined in official documents. As Hawkins and Holden (2013) point out, framing analysis has been conducted predominantly through the analysis of official written documents, such as the outcomes of policy consultations, laws, regulations and policies. This is useful material to uncover the *action frames* within official documents – i.e., the proposed policy solutions that interpret a policy problem and propose a pathway of consequential response. The definitions, terminology and the references to evidence used in these documents all contribute to the analysis of how the policy issue is *framed*. The analysis of policy and legal documents also unveiled key policy solutions and pathways of response to how a policy issue may have been framed and reframed over time. This method also served to define the problem content and the policy process – in other words, to trace the development of issue formation around the problem of poor-quality medicines.

The document analysis permitted a chronological review of policy developments aimed at addressing the problem of poor-quality antimalarial medicines, and improving access to quality essential medicines in the three national settings. Analysing the content of official policy documents provided an overview of the prioritisation of actions, and a reference point as to which pieces of evidence are deemed important or relevant in the policy making process (Hawkins & Holden 2013). The analysis of these documents helped to uncover the key steps of the policy process and the policy solutions proposed. During the analysis of documents, I

paid attention to the timeline and the authors of these documents, bearing in mind that documents are 'social facts' rather than 'representations of organization routines, decision making processes or professional dialogues' (Atkinson & Coffey 2008, p.58). I supplemented the analysis of documents with information on the policy process obtained through Method C – the semi-structured interviews. This helped to evaluate the importance of events and policy outcomes, and the role of policy actors on the policy process. The results of the document analysis provide evidence to explain the process of policy change: the occurrence of key focusing events and of key policy shifts over time. Thus, a clearer understanding of the policy process set the scene for the analysis of frames among policy actors.

5.1.3   Method C Semi-structured interviews

The third method consisted of a series of face to face semi-structured interviews with policy actors in three national settings and across institutions, as well as with global policy actors working in Access to Medicines. These semi-structured interviews were the predominant method used in the analysis of frames around the problem of poor-quality medicines (Mah et al. 2014; Hawkins & Holden 2013). The data from the semi-structured interviews helped to understand how the problem of poor-quality medicines was interpreted by key policy actors in each country, including their perceptions of determinants and challenges of this policy issue. This contributed to the delineation of the policy content and informed my analysis of the processes of issue formation around the problem of poor-quality medicines. The frames that emerged from the data also informed my understanding of the role and position of policy actors, and of the different policy solutions promoted in line with those frames. As a data collection tool, semi-structured interviews helped to explore the underlying assumptions behind actors' policy positions (Hawkins & Holden 2013) and to elucidate their perceptions, attitudes and behaviours in relation to the policy problem of poor-quality medicines (Robson 2011). By analysing how policy actors communicated their understanding of a policy problem verbally, I could reflect on what shaped their policy interests and how these interests might inform policy developments. The data also helped to understand the nature and frequency of policy actors' interactions in the policy space (Hawkins & Holden 2013). Data from these interviews was used to refine observations of the nature of the policy process and key policy shifts, and wherever possible, to source key information that supported my analysis of these processes in relation to the context. The interviews also fed into my analysis of the policy context for each case country, providing insights that would otherwise be difficult to obtain from policy documents alone.

5.2 Data collection

The data collection process occurred in three steps, repeated for each of the three case countries. For the stakeholder mapping phase (Method A), I first identified global policy actors involved in policy efforts against poor-quality antimalarial medicines from the literature review. I then identified respondents from national regulatory authorities in Cambodia, Laos and Thailand, with the help of my supervisors, advisors and partner non-governmental organisations or international organisations working on access to medicines in these three countries (Method A). Using Excel, I mapped all policy actors (individuals) and institutions involved in improving access to quality medicines in each country, including local government stakeholders, local non-governmental stakeholders and international or regional stakeholders in the three case countries. In applying this method, I used a simplified version of a stakeholder mapping exercise first introduced by Kiser & Ostrom (1982) as a method anchored in sociology. This method was then adapted by Elinor Ostrom and Paul Dragos Aligica to include terminology on policy intuitions and policy stakeholders, for its application to the study of policy developments (Aligica 2006; Ostrom 2009). The stakeholder mapping exercise was conducted in 6 steps detailed below:

1) Identifying stakeholders through literature review and expert consultation;
2) Identifying the institutional mandate of each stakeholder;
3) Positioning stakeholders within the policy space (as a local government, local non-governmental, or international and regional actors or institutions);
4) Drawing relationships and interactions between stakeholders;
5) Highlighting existing outcomes of interactions between stakeholders;
6) Refining stakeholder maps based on results from Methods B and C.

This stakeholder mapping exercise was iterative in process, as during my fieldwork I retrieved further information on policy actors, networks and their interactions from key interview respondents, building on the initial version of this map – both through the analysis of documents and the semi-structured interviews.

For the document analysis (Method B), I collected a total of 32 documents from the main institutions involved in improving access to quality medicines in Cambodia, Laos and Thailand. The criteria for the selection were as follows:

1) Policy or legal document pertaining to national or regional regulatory efforts for improving access to quality pharmaceuticals;

2) Documents publically available online since establishment of a national drug regulatory entity;

3) Documents through respondents;

4) Documents written in or translated into English.

I chose to analyse documents translated into English for feasibility reasons, and due to the limited financial resources available for translation support. Most documents were sourced from the websites of institutions identified via Method A. As it was not always possible to find up to date English translations of the relevant official policy and legal documents online, I obtained some documents from respondents during fieldwork. I crosschecked whether each document was up to date and valid with respondents during the semi-structured interviews. The types of documents analysed were:

- Policy documents: guidelines on drug quality control, or supply chain management;
- Legal documents: national drug laws;
- Public records: white papers, strategy documents, annual reports, official guidelines, progress reports.

	Cambodia	Laos	Thailand
Policy documents	1	2	1
Legal documents	7	7	5
Public records	7	0	2
Total	**15**	**9**	**8**

Table 4 Summary of documents collated per case country.

The third step of the data collection process involved travelling to Cambodia, Laos and Thailand to conduct locally-based semi-structured interviews (Method C). While in depth-interviews rely on more open-ended questions, semi-structured interviews using a pre-determined topic guide helped to steer the conversations around the specific topic of poor-quality medicines as a policy problem. Key questions were selected to guide the exploration of the problem of poor-quality medicines, in line with determinants and challenges previously identified in the literature review (Chapter 3) (The template topic guide is available at Appendix 4 on page 319). This topic guide permitted a targeted exploration of this complex policy issue.

The nature of the questions asked was occasionally altered along the data collection process, to reflect a deeper exploration of emerging themes, to clarify information, or to reflect the role and position of the interviewee. This permitted both concept-driven (using the topic guide) and data-driven data collection approaches, allowing for the identification of context-dependent themes (Green & Thorogood 2014). In essence, the topic guide provided an initial charted area of inquiry forming the basis for more exploratory discussions (Kvale & Brinkmann 2008). It also served as a checklist, with default wording and a default order of questions that varied slightly according to the country of study and the flow of the interview, in order to harness emerging themes (Robson 2011). Before leaving for fieldwork, my supervisors and advisory committee validated the topic guide by verifying the adequacy of the formulation of questions, limitations to the risk of bias, and the cultural appropriateness of the questions. I then conducted a pilot interview with a previous colleague working for the United States Agency for International Development (USAID) Regulatory Compliance Team. The colleague in question advised on the content and delivery of the topic guide and of the interview for a more adapted approach to future interviews.

As an additional tool during the semi-structured interviews, I used a map of the region to facilitate discussions on the flow of poor-quality medicines with local stakeholders. This was useful to circumvent any political sensitivity and reluctance to speak openly about the sources or the trafficking routes of these illicit goods. Participants were more comfortable when pointing towards areas at risk without explicitly voicing the trafficking routes while being recorded, and this gave them the opportunity to point and to illustrate the problem as a regional concern through visual rather than verbal means. For a politically sensitive topic, the careful choice of wording often limits their illustration of the topic.

5.2.1 Ethics

Before leaving for fieldwork, I requested ethical clearance from the London School of Hygiene and Tropical Medicines (LSHTM) Research Ethics Committee and from the health research ethics committees of the respective case countries. Ethical clearance in Cambodia, Laos and Thailand was obtained between January and August 2015 with the help of locally-based host organizations, as summarised in Table 5 below (See Appendix 5 page 320 for ethical clearance documents).

Country	Body	Host organization	Date granted
Cambodia	National Ethical Committee for Health Research	National Malaria Centre of Cambodia and Malaria Consortium in Phnom Penh	January 2015
Laos	National Institute of Public Health, Vientiane	Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit in Vientiane	March 2015
Thailand	National Research Council of Thailand	Malaria Consortium in Bangkok	August 2015

Table 5 Summary of ethical committee applications per country.

5.2.2 Fieldwork

Data collection in Cambodia, Laos and Thailand took place in three stages throughout the year 2015. The first leg took place in March and April 2015, the second leg in June 2015 and the final leg in September 2015. I stayed in the capital cities of each country (Phnom Penh, Vientiane and Bangkok), where the administrative and political centres of activity are located. Collecting data at time intervals offered the possibility to analyse data in between each leg of fieldwork and to triangulate preliminary findings through additional interviews, testing emerging themes with new respondents, as well as to explore unanswered questions and fill information gaps during my subsequent visits.

The scope of respondents approached in Cambodia, Laos and Thailand included actors with a policy mandate related to the regulation of medicines across the pharmaceutical supply chain, or actors with a mandate for law enforcement on pharmaceutical quality. I first reached out to policy actors identified through the stakeholder map, and with the help of global experts or project advisors. Before the scheduled interviews, pre-identified policy actors were sent an information sheet and consent form (in English) by email, with four anonymity options to choose from (see Appendix 6 page 324 for these documents). Further respondents were then identified and contacted while in-country through a snow-balling technique and following the recommendations of initial policy actors interviewed for this thesis. At the start of each interview, I provided a formal standardised introduction to the project (both verbally and in writing – with the information sheet). I offered to take the respondent through the consent form, if required, explaining the four levels of anonymity available to them. The level of anonymity selected by the participant dictated how I could use and quote the content of a transcript during the analysis and write up phase.

The interviews were audio-recorded for full transcription whenever the respondents consented. When the respondent declined to be audio-recorded, extensive field notes were taken during and/or immediately after the interview. Field notes also served to record impressions of the attitude of the respondent, the tone of the conversation and other observations about the speech, behaviour or gestures of the respondent useful to the process of data interpretation and analysis (Silverman 2013). While I had pre-identified locally based translators in the event that a respondent requested the interview to be in their native language, all respondents were interviewed in either English or French, without need for a translator. As I am fluent in both English and French, it was possible for me to translate interviews recorded in French during the transcription process. As French or English was often not the respondent's first language, however, the occasional lack of proficiency made the transcription process more challenging, and at times compromised the quality and perspicuity of the interview material.

5.3   Data Analysis

The process of data analysis occurred in two phases involving thematic content analysis and comparative analysis. The analysis of themes emerging from the data served as a first step to elucidate the frames that emerged both from the official documents and from the respondents' interview data. The aim was thereafter to elaborate on the dominant frames around the problem of poor-quality medicines in each country and to analyse those in view of my understanding of the policy developments before engaging in a comparative analysis of the results.

5.3.1   Thematic content analysis

I first conducted a thematic analysis of the documents collected. Each document was scanned for main themes as identified from the literature review in Chapter 3. The analysis of themes was used to identify elements of the policy process and the official definition of poor-quality medicines. I extracted key information on how poor-quality medicines were defined, on the main policy outcomes of actors' interactions as well, as information about key focusing events leading to policy changes and reforms. I note here the potential discrepancies when analysing the framings and definitions of poor-quality medicines from translated English version rather than original documents. To do so, I read each document in full twice, highlighting relevant clauses or sections of these documents that detailed the structure of the regulatory framework to improve access to quality medicines for each country. Then, I coded the content of the available legal and policy documents using an excel sheet in which I recorded recurring themes iteratively, re-arranging those throughout the process of thematic content analysis. I took note of policy developments and focusing events leading to policy change. At this stage, I was able

to cross-reference the findings from this thematic analysis with the map of stakeholders, highlighting where and how actors and networks influenced policy developments. The findings gathered from this phase of the analysis are represented in each results chapter as a chronological narrative of the policy process, and illustrated through a timeline. I also paid specific attention to the use of terminology in each document, making note of the definitions of poor-quality medicines. This process provided an indication of how the problem for poor-quality medicines was conceptualized in official documents, as material for reflection on how the official definitions might influence policy developments. The outcome of this analysis is represented in the form of a table of official definitions for each country.

I then conducted a thematic content analysis of the data from the semi-structured interviews against the themes emerging from Chapter 3. The analysis of themes here served to identify key determinants and challenges of the issue of poor-quality medicines as perceived by policy actors, and to discern contextual factors that might influence policy developments. I followed five main steps in the thematic content analysis process, from data familiarization, coding, indexing, charting and mapping to data interpretation (Ritchie & Spencer 1994). Recordings of interviews were first converted into time-stamped transcripts that were uploaded into a Computer-Assisted Qualitative Data Analysis software (Nvivo 10), along with word-processed field notes. After the transcription process, which served as a phase of data familiarization, the main themes were coded along a pre-determined coding framework, created from the list of themes and the conceptual framework emanating from the literature review (See Appendix 7 on page 328 for coding framework). This coding stage involved a tagging process using highlighting tools to identify key themes from the data (Pierce 2008). While the initial coding framework was based on the themes identified in the literature review, the analysis phase gave special attention to themes that emerged from the data as 'free nodes' (Glaser & Strauss 2008).

To identify key themes and causality references in this coding stage, I paid specific attention to key terms such as 'because', 'after', 'then', 'same as', where participants shared their perceptions and experiences of the policy issue (Green & Thorogood 2014). This information also contributed to my understanding of the policy process and the policy context. Nvivo 10 software facilitated the management of data permitting easier navigation between cluster of themes (Spencer *et al.* 2014; Green & Thorogood 2014). I conducted a comprehensive analysis of the data until no new themes emerged that had not already been taken into consideration (Silverman 2011). This stage of the thematic content analysis process served to highlight what determinants and challenges policy actors attribute to the policy issue of poor-quality

antimalarial medicines. These findings were then coded as a final list of themes and sub-themes for each country.

The indexing phase involved a deeper theoretical reading of these emerging themes (Kvale & Brinkmann 2008), during which I was able to draw key observations on stakeholders' perceptions of the policy issue. I matched the emerging themes to the pre-determined list of frames. To do so, I used the pre-set list of six 'master' frames (as identified in Chapter 4), which allowed for a more systematic and meaningful comparison of framings of the problem of poor-quality medicines across countries. This process helped to refine the list of frames iteratively and in accordance with the themes emerging from the data. During this indexing phase, I applied a method of 'constant comparison' in order to spot patterns in the data (Glaser 1999; Pierce 2008; Green & Thorogood 2014). As a result, I identified salient themes among all three categories of respondents and paid specific attention to those that bore the most references. From the data, I depicted both rhetorical frames (the debates and stories in relation to the policy issue) and action frames (evidence of practice, policy solutions, laws or policy) (Schön & Rein 1994). I referred to both the content of the transcripts and my field notes in order to depict the specific attitudes of local stakeholders towards the policy problem (Chong & Druckman 2007). This helped to capture the tone of the discussion and elements of the social context that may influence the data. I paid particular attention to the terminology used by respondents, their specific definition of the problem and the rationales used repeatedly by local respondents from each country to explain this problem. I created a separate coding scheme in Nvivo for these dominant or 'master frames' used across and within all three categories of respondents.

The fourth stage (charting) involved drawing linkages between the master frames, and the dominant themes emerging from the data that describe the substance of each dominant frame. I charted different interpretations of the policy issue across institutional settings (across the three categories of respondents) within the same frames. By juxtaposing the framings that emerged from the document analysis and the interview data, I was able to explore the implications of perceptions of the problem for policy developments to improve access to quality medicines within each country. The results from the thematic analysis of the interview data are presented separately for each case country, as a thematic narrative describing the six frames in detail and acknowledging variations in interpretations of the policy issue across institutional setting, while reflecting on analogies between actors' perceptions and recent policy developments.

The limitation of thematic content analysis for the study of frames is that the classification of frames by the researcher is itself a subjective process – a limitation which I have sought to address through a reflexive data collection and analysis process. More specifically, I followed an iterative process of data collection and analysis based on the Spiralling Research Approach by Berg & Lune (2012), as illustrated in Figure 7 on page 92. This approach is particularly adapted to the nature of this study which required a strong awareness of the socio-political context, as it provided an opportunity to adapt data collection tools throughout the data collection process (Green & Thorogood 2014; Berg & Lune 2012). The Spiralling Research Approach is inherently reflexive and allowed for Methods A, B and C to feed into one another throughout the data analysis process. For example, while the stakeholder mapping (Method A) supported the data collection process for Methods B and C, both the data from the analysis of documents (Method B) and from the interviews (Method C) helped to refine the maps of stakeholders.
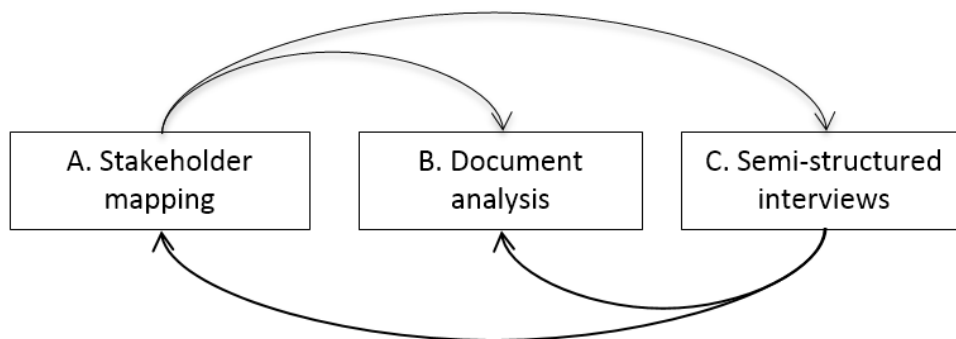
Figure 7: Research methods in a reflexive research process

Cross-feeding between the findings of Methods B and C was useful to triangulate findings and develop my observations of the level of enforcement of written policies and laws. The data from the interviews helped to verify the findings from the analysis of official documents – enhancing my understanding of the policy process. I ensured that the research design per se remained unchanged through maintaining careful awareness of the data collection and a systematic process of data analysis. In practice, therefore, the spiralling research approach allowed for the refinement of the criteria for the document analysis and the topic guides for subsequent semi-structured interviews, with the aim of delving deeper into emerging themes without drastically altering the systematic application of each method.

5.3.2 Comparative analysis

After the analysis of the main themes emerging from the document analysis and the semi-structured interviews, and exploring how these inform our understanding of the policy process and the analysis of frames of the problem of poor-quality medicines, I proceeded to undertake a comparative analysis of the policy processes and frames used by respondents across the three case countries. This was conducted in two phases.

First, I reflected on the similarities and differences in the policy development processes and how comparable the policy solutions to address the issue of poor-quality medicines were. I noted whether, in the chronological progression of policy efforts between these three countries, there was evidence of policy coherence, overlaps of initiatives, or evidence of policy transfer between one context to another. I also reflected on potential gaps in policy processes from one country to the next, and the role of policy actors and how different categories of actors, or actor configurations influence the policy process in the three countries. The comparative analysis process was made easier with the visualisation of the policy processes in a timeline format. I then compared the dominant framings of the problem of poor-quality antimalarial medicines in Cambodia, Laos and Thailand. Through the mapping & interpretation stage of the thematic content analysis approach, I charted the similarities and differences between the five dominant frames and the sub-themes emerging from the data across the three countries. I noted the similarities and differences in official definitions of 'poor-quality medicines' across the three countries in the policy and legal documents. I compared how different policy actors, across institutional and national settings, defined the policy issue and if relevant, I depicted variations in how the same frame was articulated across the three countries. This was done by juxtaposing the list of themes and subthemes that emerged from the data, and investigating how these reflect different articulations of each frame.

Comparative analysis offered the opportunity to improve the reliability of my observations from the data. I compared these observations across national contexts to uncover any discrepancies in my empirical analysis. In this process, I also referred to the data from global expert interviews to inform the arguments in the final discussion of findings. Besides these triangulation methods, I sought to improve the reliability of my findings by cross-referencing them across the three methods. Respondents' contributions cannot be considered to be flawless reflections of reality, and their accounts had to be interpreted carefully and in light of other information obtained through document analysis, or from the literature.

I also made sure that all of the data was coded comprehensively, ensuring that disconfirming evidence and deviant cases are addressed and included in the analysis (Green & Thorogood 2014; Silverman 2011). Additionally, I consulted my supervisors and the advisory committee on certain batches of data and their coding structures. This ensured the reliability of my analytical framework and demonstrated that the codes and thematic structure that emerged from the data were not solely reliant on my subjective analysis (Green & Thorogood 2014). To ensure the validity of my findings, I also sought to obtain validation of my findings from respondents whenever possible, by going back to participants and asking them if findings seemed relevant and accurate (Green & Thorogood 2014). This was a useful approach, especially as it provided an opportunity to verify elements of confidentiality with the participants who could approve or reject quotations extracted from their accounts, when applicable. This method also offered the possibility to share some key findings and recommendations with the decision makers that were interviewed in the data collection phase of this study, as an organic reporting mechanism.

Introduction to results

Respondents

A total of 51 respondents[30] were interviewed during my fieldwork in Cambodia, Laos and Thailand. Before leaving London, 23 key informants were first identified through the stakeholder map exercise and some initial contacts on the ground were made with the help of my research advisors based in Southeast Asia. A further 30 were recruited while in the field, identified through snowballing technique following recommendations from interviewees. This respondent-driven approach was iterative and largely driven by data refinement (Ritchie et al. 2014). It offered the possibility to address information gaps when required and was well-suited to the exploratory nature of this study which delves into a politically-sensitive and complex, multi-faceted phenomenon.

Table 6 on page 96 summarises the number of respondents per country and for each category of respondent. Under 'government-level respondents', I include representatives from the Ministry of Health, National Regulatory Authorities (NRAs), national malaria control programs and law enforcement institutions such as customs or police. 'Non-government respondents' include local civil society, local representatives from academia or from the industry, in-country representatives from donor organisation, inter-governmental organisations or international non-government organisations based locally, some of which were key implementing partners in the policy process. Under non-government respondents, I was also able to interview three industry representatives. They were included in the sample of respondents so far as they were involved in the agenda-setting process, and because the opportunity presented itself by referral. The sample of respondents did not include patients. However, respondents in each country shared interpretations of consumer behaviour as a contributing factor to the illicit trade in poor-quality antimalarial medicines.

Country	Respondents	No.	Total
Cambodia	Government-level	2	17
	Non-government	15	
Laos	Government-level	9	17
	Non-government	8	

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[30] A full list of respondents is available in Appendix 8 on page 330

Thailand	Government-level	7	17
	Non-government	10	

Table 6 Number of local respondents per sector, per country.

Simultaneously, in the course of the year 2015 and 2016, I conducted semi-structured interviews with 23 international experts on access to quality essential medicines, in order to gauge their opinion on the complexity of the issue and on the factors they believe contribute to the prevalence of falsified essential medicines globally. Most of interviews with experts were conducted by tele-conference, although five of those were conducted in person. As summarised in Table 7 (page 96), the sample of expert respondents included senior members of international non-government, inter-governmental and donor organisations, representatives from the pharmaceutical industry, as well as academics and one respondent from the media. The results from these interviews served to inform the research design and triangulate findings in the discussion chapter.

Category of Expert Respondents	No. of Respondents
International Non-Governmental Organisations	6
Inter-Governmental Organisations	2
Donor Organisations	2
Pharmaceutical Industry	5
Academia	7
Other (media)	1
Total	**23**

Table 7 Number of expert respondents per sector

Interviews were conducted in English and a few in French. All local policy actors were proficient in either language. Medical or pharmaceutical studies in Laos for example are offered mainly in French. In their role, most local policy actors re are required to work collaboratively with counterparts from other countries, in English. For these reasons, no interpreter was required for the interviews. As a French educated in English speaking countries, I was comfortable conducting interviews in either language.

Data management and anonymity

Various respondents clearly expressed their fear at associating their name or that of their organization to this sensitive topic, as this might affect their professional relations or personal safety. For this reason, effective data management and preservation of anonymity were key concerns through the data collection and analysis process. there were four categories of anonymity as described in the consent forms shared with respondents ahead of the scheduled interview. A total of only 25 respondents provided full consent, and a total of 12 respondents refused for the information to be cited directly. The reasons provided for refusing to be cited as part of this study were to preserve close working ties with government officials in country, because of non-disclosure agreements under donor polices, or because of fears of disapproval from senior management. As most respondents requested that their contributions anonymized and only few agreed to be quoted directly, I chose to anonymise all quotations in the results chapters.

Color Code	Consent Type
GREEN	1
BLUE	2
ORANGE	3
RED	4

Consent type 1. Respondent agrees to take part in this interview and for quotes and other material arising from his/her participation to be used and attributed by name. *(Note some individual statements were still requested to remain anonymous during the interview.)*

Consent type 2. Respondent agrees that material from my interview may be quoted, but would like his/her name to be anonymised.

Consent type 3. Respondent agrees that material from my interview may be quoted, but would like his/her name to be anonymised as well as any other information that might be used to identify him/her, including the organisation that employs him/her.

Consent type 4. Respondent does not agree for any material from the interview to be quoted but the researcher may use the information from the interview to inform her analysis.

To guarantee the anonymity of respondents and respect confidentiality levels, each respondent is attributed a unique code, used to reference quotations and statements in the results chapters. The master sheet with the respondent codes and corresponding respondent information is kept in a secure password-protected folder on my computer. The information about respondents has been omitted from all published documents when anonymity was requested, ensuring that no additional information could accidentally reveal the identity of the respondents (i.e. institution, name of department etc.). Additionally, each interview recording was re-named with the numerical code assigned to the respondent. To keep track of anonymity requirement, each respondent and matching transcript was given an anonymity colour code. In the numerical code for each respondent, STK stands for locally based policy actors across all categories. EXP stands for expert respondents interviewed outside the three countries. Each stakeholder and expert respondent was then given a number from 01 onwards, in chronological order. References for each respondent's contribution includes the category of the respondent and the date of the interview. For example, the seventh stakeholder interviewed (07) was a respondent from a national regulatory authority, interviewed on the 1st of April 2015. The code attributed was therefore STK07G_NRA20150401. I use this numerical code structure to reference inputs from respondents in the results chapters.

All recordings were stored in a password-protected folder and removed from the recording device. The data collected is stored in a secure encrypted folder, using the software 7-zip. Data which was stored on my personal laptop during fieldwork was immediately transferred to the secure LSHTM server upon my return to London. To ensure that no data was accidentally lost, it was also stored on a password protected folder on Filr and on an external hard-drive securely stowed in a locked drawer at LSHTM. This data will be stored on a secure platform for a minimum of ten years following study completion, in accordance with the Retention and Disposal schedule of LSHTM.

The categories of respondents are attributed as follows:

G – Government
NG – Non-Government
NRA - National Regulatory Agency
NMCP - National Malaria Control Program
MoH - Ministry of Health
LEA - Law Enforcement Agency
IGO - Inter-Governmental Organisation

INGO - International Non-Governmental Organisation

LNGO - Local Non-Governmental Organisation

Donor - Donor Organisation (or Country)

Academia – Academia

Consult - Consultant

Pharma - Pharmaceutical Manufacturer (or Association)

Country	Category	Organisation Type	Organisation Names
Cambodia	G	NRA	Department of Drugs and Food (1)
		NMCP	Cambodia National Malaria Center (1)
	NG	IGO	World Health Organisation Country Office (2), United Nations United Nations Office for Project Services (1)
		INGO	Malaria Consortium (1), Clinton Health Access Initiative (1), Population Services International (1), United States Pharmacopeia (1), ACT Watch (1)
		LNGO	Cap Malaria (1). University Research Cambodia (1)
		Donor	Australian Department of Foreign Affairs and Trade (1), United States Agency for International Development (2), France Fond Solidaire Prioritaire Mékong (1)
		Consult	Independent health consultant (1)
Laos	G	NRA	Food and Drug Department of Lao (6)
		NMCP	National Center of Malariology, Parasitology and Entomology (1)
		MoH	(1)
		LEA	Customs (1)
	NG	IGO	World Health Organisation Country Office (2)
		INGO	United States Pharmacopeia (1)

		Academia	Lao-Oxford Mahosoty Medical Research Unit (2), Worldwide Antimalarial Resistance Network (1)
		Donor	Anonymous (1)
		Pharma	Domestic Manufacturer (1)
Thailand	G	NRA	Thai Food and Drug Administration (2)
		NMCP	Bureau of Vector-Borne Diseases (1)
		MoH	Bureau of Drugs and Narcotics (1)
		LEA	Customs (2), Police (1)
	NG	IGO	United Nations Office for Drugs and Crime (1)
		INGO	International Organisation for Migration (2)
		LNGO	PhraRed (1)
		Academia	Chulalongkorn University (3)
		Pharma	PreMa (1), Local Manufacturer (2)

Presentation of results

The next three chapters present the results for Cambodia, Laos and Thailand in three separate chapters (6-8). Each empirical chapter starts with an introduction to the historical and political context of the country. This background section provides a brief overview of the health system in each country of recent reforms and of the main policy documents regulating pharmaceuticals. It also provides a short introduction to the malaria burden situation in each country. The second section of the empirical chapters offers a chronological overview of the policy processes to improve access to quality medicines and to reduce the circulation of poor-quality AMLs in Cambodia. This is represented in the form of a timeline. The narrative around this timeline is informed by the results of the document analysis and supplemented, where necessary, with data from interviews and from the literature. For each country, I include more information about the regulatory system for each country – by regulatory function. This information is available in the Appendices (Appendices 9, 12, 15). The stakeholder mapping provides an overview of a dynamic network of actors. I present information on these policy actors in a table format which is available in the Appendix section (Appendices 10, 13, 16). Gathering information on all the partners was useful for both the data collection and analysis processes of the thesis. The relationships between the policy actors were too complex to represent visually. However, where relevant, I do include a diagram of their interactions over

a specific program (as in the case of Cambodia). These visual representations only represent a snap shot in time however and the network of policy actors is as dynamic as the issue of poor-quality medicines is complex. The third section of the empirical chapters presents the results from the semi-structured interviews conducted with policy actors on site. I present the main themes alluded to by government and non-government level respondents under each of the six frames that reflect policy actors' perceptions of the problem of poor-quality medicines - its drivers and challenges. For each country, this section provides an overview of which frames were most prevalent among government and non-government respondents. The last section of each empirical chapter summarises respondents' interpretations of the challenges and main contributing factors to the problem of poor-quality AMLs. In this last section, I reflect on the implication of findings for policy development in each country.

Chapter 6   Cambodia Results

6.1   Background

Figure 8 Map of Cambodia (Source: World Health Organization & MoH Cambodia, 2012)

Cambodia, officially known as the Kingdom of Cambodia, is a constitutional monarchy bordering Thailand, Laos and Vietnam, with coastlines to the south-west on the Gulf of Thailand (see Figure 8). Both the Tonle Sap and the Mekong River flow through Phnom Penh, the capital city, where most government institutions reside, including the Ministry of Health (MoH). Currently, there are 25 provinces divided into 163 districts (*srok*), that are in turn made up of communes (*khum*). Cambodia gained independence from France in 1953. The Communist Party of Kampuchea (whose followers were known as Khmer Rouge) ruled between 1975 and 1979, marking a period of total social transformation of the country into a 'prison farm' (Chandler 1991, p.239). The initiation of the Khmer Rouge regime led by Pol Pot, caused extreme suffering under a highly centralized ruling system, resulting in up to 2 million deaths from warfare, overwork, executions, disease, and starvation (Chandler 1991). And then, following the fall of the Khmer Rouge regime and the Vietnamese occupation, came a period of civil war. It is only after decades of social disruption that Cambodia has recently entered a period of economic growth and more political stability. The foundations of the current political system were established in 1993, when the first elected government drafted

the Constitution of the Kingdom of Cambodia. The political system remains largely centralized, although some efforts to introduce administrative and political decentralization are underway (World Bank 2005).

Indicator	Value	Year (Source)
Total Population (million)	15.6	2015 (WB)
Gross Domestic Product - Purchasing Power Parity (International $)	3,483	2015 (WB)
Human Development Index (HDI)	0.555 (Rank 143)	2015 (UNDP)

Table 8 Cambodia economic and development indicators

Cambodia has been a member of the Association of Southeast Asian Nations (ASEAN) since 1999, and a member of the World Health Organization (WHO). It falls within the lower-middle income country (LMIC) category as defined by the World Bank, although its economic expansion has been relatively robust of late, with yearly growth at an estimated 7% relying predominantly on its textile industry, the tourism industry, as well as the construction sector (Asian Development Bank 2015a). While poverty rates halved between 2007 and 2012 (from 47.8 to 18.9%), there is still high income inequality, especially between urban and rural populations (BMI Research 2016). Cambodia ranks 143rd on the Human Development Index. The working population of Cambodia is highly mobile, with migrant workers' movement driven by economic concerns towards border areas, where land development projects in farming and mining abound (Bourdier 2010).

6.1.1 The Cambodian health sector

Early efforts to introduce public health and sanitation in Cambodia date back to the French colonial period. During the Khmer rouge regime, however, the healthcare system was severely weakened. Significant reforms took place from 1990s onwards to strengthen the system anew. Since the 1990s, Cambodia operates a de-centralized governance health service delivery approach, through 24 Provincial Health Departments and 81 health Operational Districts (Annear *et al.* 2015). Despite substantial reforms and a relatively high health expenditure in part due to external support of donor organizations (at 5.7% of GDP), life expectancy in Cambodia remains below the East Asia and Pacific regional average of 74, at 68 years (World Bank 2014a). Moreover, despite health financing mechanisms introduced in the early 2000s,

Cambodia still has one of the largest out-of-pocket expenditures in Southeast Asia, including for medicines (ACTwatch Group & PSK 2014).

Indicator	Value	Year (Source)
Total Health Expenditure (% of GDP)	5.7	2013 (WB)
Heath expenditure per capita (current US$)	61	2014 (WB)
Out-of-Pocket Health Expenditure (% of Total Health Expenditure)	74	2014 (WB)
Physicians per 1000 population	0.2	2012 (WB)
Pharmacist per 1000 population	0.01	2012 (IFP 2012)
Life expectancy	68	2014 (WB)

Table 9 Cambodia health indicators

The Cambodia Heath Strategic Plan II (HSP II 2008-2015) drove the recent health sector reforms, and was designed to improve primary healthcare coverage (MoH Cambodia 2008), by promoting equitable access to health services and optimizing the allocation of resources to provincial health departments (WHO 2011). Despite the reforms planned under HSP II, access to quality healthcare and medicines currently remains patchy. Low salaries in the public health sector mean that many health workers seek to supplement their incomes by working in the private sector. This dual practice affects the quality of care available, as public health facilities suffer from recurrent unavailability of staff and long waiting times (Annear *et al.* 2015). Rural and remote communities have a significant shortage of certified medical personnel (Annear *et al.* 2015). This has been one of the various factors that have influenced patients' negative perception of the quality of public health services. It is estimated that over 67% of patients first seek treatment from the private sector including private pharmacies (Kosal *et al.* 2015). Traditional healers are also widely respected in Cambodia and 50% of the Cambodian population relies on traditional medicines for treatment of less serious illnesses (Sokhieng 2011; WHO & MoH Cambodia 2012). With regards to the pharmaceutical sector, there is currently a reported low density of licensed pharmacies per 1000 population (0.1) (International Pharmaceutical Federation 2012). Most pharmacies are run by non-pharmacists (Khan, Okumura, *et al.* 2011; Fougeres 2011) and unlicensed private sector drug outlets are largely prevalent in provinces outside Phnom Penh (ACTwatch Group & PSK 2014).

6.1.2   Regulating antimalarial medicines in Cambodia

The main laws regulating pharmaceuticals in Cambodia are the Royal Kram (Law) on the Management of Pharmaceuticals (1996) and its Amendment (2007). Appendix 11, page 350 summarizes information retrieved from a thematic content analysis of 15 Khmer law and policy documents translated into English. The MoH is responsible for the regulation of pharmaceuticals through the Department of Drugs and Food (DDF). The DDF has five separate bureaus with different functions, as summarized below (see Table 10 p.106). The Drug Regulation bureau and its provincial counterparts hold the mandate for the licensing of pharmaceutical outlets. There are three types of public sector pharmaceutical outlets in Cambodia, including Pharmacies, Depot A and Depot B outlets. In theory, Depots A and B pharmacies are set up when and where there is a lack of licensed pharmacy outlets in any given area. The Prakas on the Formalities and Conditions for Opening /Closing /Relocation of a Pharmaceutical Selling Establishment (2009) briefly addresses the problem of poor-quality medicines, and states in Article 25 that pharmacists are not allowed to 'display medicines from illegal sources for sale; display medicines with no label for sale'. By using the word 'display', the implementation of this clause is uncertain, as medicines from illegal sources could be kept hidden and brought out on request without infringing on the law. Control agents within the MoH are responsible for inspecting and seizing poor-quality medicines in pharmacy outlets. The (2011) Prakas on Roles and Responsibilities of Control Agent (Article 8) mandates MoH control agents to seize 'counterfeit medicines, medicines which are banned by MoH, medicines without license… and other suspicious exhibits'. This Prakas places counterfeit, expired, unauthorized, and unlicensed medicines (such as oAMTs) under the same definition. The term 'other suspicious exhibits' adds ambiguity as it might also encompass substandard medicines. The Prakas does not specify how 'counterfeit' or 'suspicious' exhibits are to be differentiated or tested for. For more information on Cambodia's pharmaceutical regulatory system, refer to Appendix 9 on page 340.

Departments	Functions and Roles
Narcotic Control and Pharmaceutical Trade Bureau	Licensing of pharmaceutical companies Registration of import/export companies Registration of traditional medicines
Drug Regulation Bureau	Development of drug legislation, regulations, policies and guidelines (e.g GMP) Conducts regulatory inspections Control drug advertisements

Registration and Cosmetic Bureau	Oversees drug registration process
Essential Drugs Bureau	Promotes rational drug use Ensures adequate supplies for public sector
Food Safety Bureau	Regulates food products

Table 10 Functions of the Cambodia Department of Drugs and Food

The National Centre for Entomology, Parasitology and Malaria Control (CNM) is responsible for Cambodia's malaria program and is involved in the procurement of ACTs in Cambodia. CNM decides on the required quantity of ACTs at a given time. The medicines procurement process is rarely made public in Cambodia, thus enabling only limited operational transparency within the Essential Drugs Bureau (WHO, 2008). This may have been part of the reason why CNM was audited for mismanagement of GF funds and thereafter lost its status as principal recipient of the grant to UNOPs. Additionally, there are reported gaps in the process of medicine distribution. Further studies suggest that the current supply chain of AMLs is complex and therefore difficult to regulate, making it challenging to monitor the quality of health products. With regards to the sale of AMLs for example, ACTwatch (ACTw 2014) reports that 60% of all AMLs outlets surveyed came from private sector outlets including pharmacies (20%), itinerant drug vendors (14%) and private for-profit facilities (12%). Adding to this busy landscape of pharmaceutical outlets, national malaria treatment guidelines change regularly, thus making it hard for licensed outlets to follow the regulations, procure and dispense the right treatments. The same ACTw report (2014) also suggests that the supply chain for essential medicines is heavy on wholesalers who trade among themselves, therefore creating a complex multi-entry-point supply chain. This makes the task of regulating the entirety of the formal and informal supply chain for AMLs a complex one.

With regards to malaria, while Cambodia has been successful at reducing incidence rates of malaria between 2000-2015 by 50–75% – from 76,000 cases in 2003 to 25,152 confirmed cases in 2015 (WHO, 2015) – disease transmission persists in the hard-to-reach tropical forest areas. Although malaria no longer represents a major health concern in central Cambodia, transmission zones remain in border and forest areas which represent about 48% of Cambodia's land mass despite extensive deforestation (Open development 2016). Both *Plasmodium falciparum* (61%), *Plasmodium vivax* (39%) malaria are present in Cambodia (WHO 2016). Malaria, known as 'forest fever'[31] in Cambodia, is transmitted by mosquitoes

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[31] Another local term used in Cambodia is '*krun chanh*' or 'fever with chill'.

that breed in forests and jungles (Guyant *et al.* 2015). An estimated 44% of the population, or approximately 6.3 million people, live in high transmission areas (ACTwatch Group & PSK 2014).

The population most at risk are mobile and migrant populations (MMPs), including 'forest-goers' – that is people who travel to and may stay overnight in the deep forest while doing activities such as logging, bamboo cutting, charcoaling, and foraging (Bhumiratana *et al.* 2013; Guyant *et al.* 2015). MMPs are also at higher risk as they are generally socially, geographically and economically marginalized with limited access to health services and medicines (United States Agency of International Development 2014). Resistance to artemisinin-based malaria treatments was first found along the Thai-Cambodia border in 2006 and reported in 2008 (Noedl *et al.* 2008), although the WHO Global Malaria Programme suggests that resistance likely emerged as early as 2001 (WHO 2014). This region was also the epicentre of resistance to chloroquine in the 1960s (Bhumiratana *et al.* 2013). According to ACT Watch (2014), the unregulated sale of oAMTs, the limited access to ACTs and the availability of poor-quality AMLs might have contributed to the rise in artemisinin resistance. Artemisinin resistance is an added dimension to the complicated landscape of malaria control and elimination in Cambodia.

The Global Fund to Fight Aids, Tuberculosis and Malaria (GF) has disbursed over USD 121 million to date in support of the malaria program (The Global Fund 2015). The United Nations Office for Project Services (UNOPS) Cambodia office manages the GF grant as the principal recipient (PR) and a main actor in the procurement of ACTs along with CNM. Cambodia was the first to make a country-wide switch to ACTs as the first-line treatment for uncomplicated malaria in 2000, and to implement a national ban on the import and distribution of oAMTs in 2008 (WHO 2015). The current first-line treatment for malaria in Cambodia is Artesunate Mefloquine (AS+MQ) and Dihydroartemisinin Piperaquine (DHA-PPQ+PQ). In case of treatment failure, Quinine Tetracycline (QN+T) is used (WHO 2015). ACTs funded by the GF are available for free from public health providers which include public health facilities, pharmacies as well as VMWs. However, private providers still play an important role in the treatment of malaria (Patouillard *et al.* 2011).

6.2   Policy developments against poor-quality AMLs

From my analysis, I discern three distinct phases in the policy process against poor-quality AMLs in Cambodia. Between 2000 and 2005 was a phase of issue formation around the

problem of poor-quality AMLs, whereby policy actors[32] collaborated to gather evidence about the prevalence of poor-quality AMLs. The problem of poor-quality medicines had reached the policy agenda by 2005. Then followed a period of capacity building efforts, spearheaded by international implementing organizations offering technical assistance. Subsequently, policy developments around poor-quality medicines have largely been guided and influenced by growing concerns with the emergence of artemisinin resistance in Cambodia's border provinces. There was a clear shift in policy approach in the year 2010, leading to greater emphasis on post-marketing surveillance (PMS) and pharmacovigilance (PV) efforts. This was mainly to enforce the ban on Oral Artemisinin Monotherapies (oAMTs), which contribute to the spread of artemisinin-resistant malaria. The timeline available on page 109 (see Figure 9) provides a chronological overview of the laws and policies introduced over time to regulate pharmaceuticals and their quality in Cambodia.

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[32] For an overview of policy actors in Cambodia please refer to Appendix 10 page 343
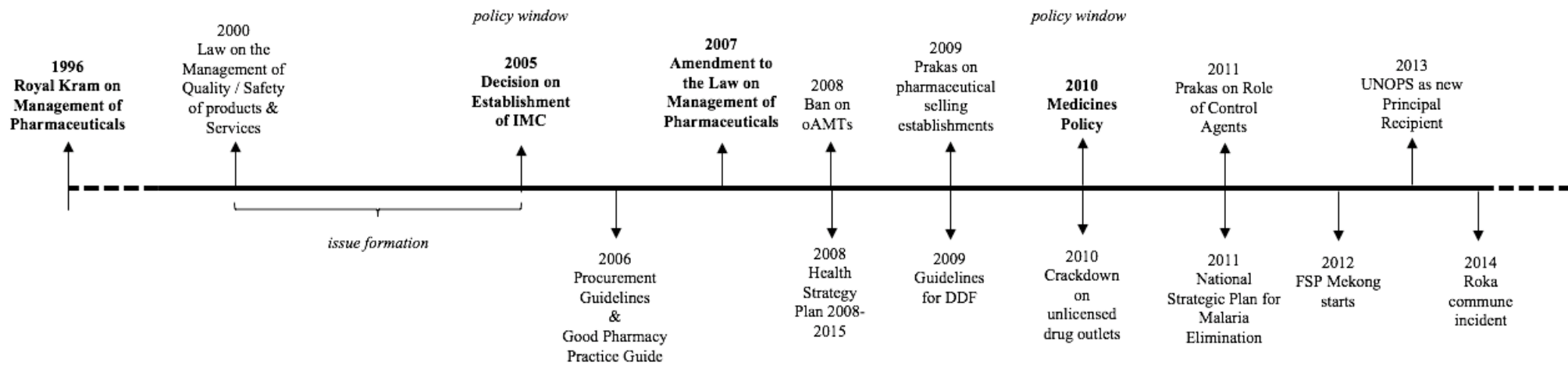
Figure 9 Timeline of policy developments for pharmaceutical regulation in Cambodia

6.2.1   Phase I: Evidence gathering and issue formation (2000-2005)

6.2.1.1   The role of evidence

Evidence of poor-quality AMLs in Cambodia contributed to the initial process of issue formation. The presence of poor-quality AMLs in Cambodia was first reported in 1999 in a survey by the European Commission-Cambodia Malaria Control Project on artesunate in the private sector. This survey highlighted that 71% of artesunate tablets and 60% of mefloquine tablets from 133 drug outlets in 8 provinces were of poor-quality (Rozendaal 2001a). In another study, Newton and colleagues (2001) reported that 25% of artesunate tablets collected in Phnom Penh and Seam Reap contained no active ingredient. In response to this new evidence, Cambodia introduced its very first ACTs by packaging Artesunate and Mefloquine tablets in-country (A+M) and distributing those to patients (Yeung *et al.* 2015). The WHO in Cambodia, the United States Pharmacopeia (USP) and the MoH of Cambodia conducted two surveys to better understand the nature of this threat. In 2001 and 2004, the MoH and the WHO conducted studies on 'counterfeit and substandard drugs in Cambodia' and reported a prevalence of 10.43% (2001) and 21.13% (2004) in 'counterfeit' essential medicines, including oAMTs as well as analgesics and antibiotics (MoH Cambodia 2001, 2004). It is unclear how and to what extent these pieces of evidence have been used in policy making and programme implementation. However, a number of developments in the early 2000s indicate increasing attention to this problem. For example, from 2003 onwards, technical assistance partners including Population Services International (PSI) and United States Pharmacopeia (USP), set up two initiatives in 2003 onwards that would prove crucial in supporting the Cambodian government's efforts against poor-quality AMLs. Arguably, this information might have contributed to an initial process of issue formation, where government officials progressively came to the realization that poor-quality AMLs were of concern in Cambodia.

6.2.1.2   Technical assistance partners

PSI and USP both actively contributed to raising awareness about the importance of drug quality monitoring, and proposed tangible policy initiatives to prevent the circulation of poor-quality medicines and improve access to quality assured ACTs. USP supports the DDF on quality control operations of key AML samples since 2003 through the Drug Quality and Information (DQI) program, which was renamed the Promoting Quality of medicines (PQM) Program in 2009. Backed by USAID, USP uses the Global Pharma Health Fund (GPHF)

Minilab[33] to perform field quality checks in 13 sentinel sites. It also provides training and equipment to strengthen the capacity of the national quality control laboratory as a concrete step towards strengthening the government's capacity to control the quality of essential medicines. The PQM program provides technical assistance for post-marketing surveillance activities (Krech *et al.* 2014) and is implemented in collaboration with DDF, the MoH, the IMC, and other international partners including the WHO, the French Foreign Affairs' Fonds de Solidarité Prioritaire (FSP Mekong), INTERPOL, and the Global Fund (Krech *et al.* 2014). As a result of quality control activities under the PQM program, the MoH released official bans on the importation and sale of products from manufacturers whose products were deemed of poor-quality (Krech *et al.* 2014).

PSI works hand in hand with CNM and DDF on harnessing the private sector as a legitimate distribution channel for quality AMLs through their social marketing scheme (the PPM program). The Public-Private Mix Strategy (PPM by PSI) was first set up in 2003 by CNM, with the help of the international health organization and product development partnership PATH and Management Sciences for Health (MSH). PPM was set up to encourage certification of private drug sellers and to strengthen malaria diagnosis and treatment options in Cambodia's private sector. PSI now works in close cooperation with CNM to implement the PPM Strategy. Malarine (Artesunate Mefloquine) is now sold at subsidized prices in private outlets trained through the PPM program. Considering the high percentage of patients seeking treatment from the private sector in Cambodia, respondents agree that the PPM strategy has been an important initiative since 2003 to improve access to more affordable quality medicines in the private sector, and to reduce the number of poor-quality medicines reaching patients. Through both the PPM and the PQM initiatives, PSI and USP were key policy actors in this first phase of issue formation and eventually, interest formation.

6.2.2 Phase II: Interest formation around artemisinin resistance (2005-2010)

6.2.2.1 The IMC: institutionalizing efforts against counterfeit and substandard medicines

This second phase starts with a network configuration change and the establishment of the Inter-Ministerial Committee to Fight against Counterfeit and Substandard Medicines (IMC) in 2005. Further evidence emerged in 2003 and 2006 confirming that poor-quality antimalarials were still a problem in Cambodia. Lon and colleagues (2006) reported that 57.9%

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[33] The GPHF minilab: Developed by the Global Pharma Health Fund E.V., the minilab was designed to provide all the basic testing tools of a laboratory in one suitcase. It is used to test the quality of medicine samples in resource-constrained and remote areas, where laboratory access is limited.

of antimalarial tablets surveyed from licensed outlets and 75.2% from unlicensed outlets were found to be of poor-quality, with products labelled as being from Thailand, China, Cambodia and Vietnam, amongst others. The IMC was established as a coordination hub for the exchange of information across ten ministries for targeted efforts against poor-quality medicines (see Figure 10 page 113 for a visual representation of the committee membership). It was intended to serve as a platform to raise awareness across departments about this threat and facilitates the cooperation of health control agents, police and customs officials in fighting against the trade of poor-quality and unauthorized pharmaceuticals. Respondents suggest that the Ministry of Economy and Finance (MoEF) has a strong influence in this coalition, due to the power that it holds over approving the budget of the MoH. Aside from the MoH and the MoEF, the Ministry of Justice (MoJ) plays an important role in harnessing support against 'counterfeit' medicines through the IMC, as it oversees criminal law against pharmaceutical crimes. There is no evidence in this study of any such penalties being implemented, however. The Ministry of Interior (MoI) within the IMC, coordinates the involvement of customs and police officials in the fight against poor-quality medicines in general. The IMC represents an important network configuration change to trigger regulatory responses against poor-quality medicines. The establishment of the IMC evidences that by 2005, the problem of poor-quality medicines had reached the policy agenda in Cambodia.
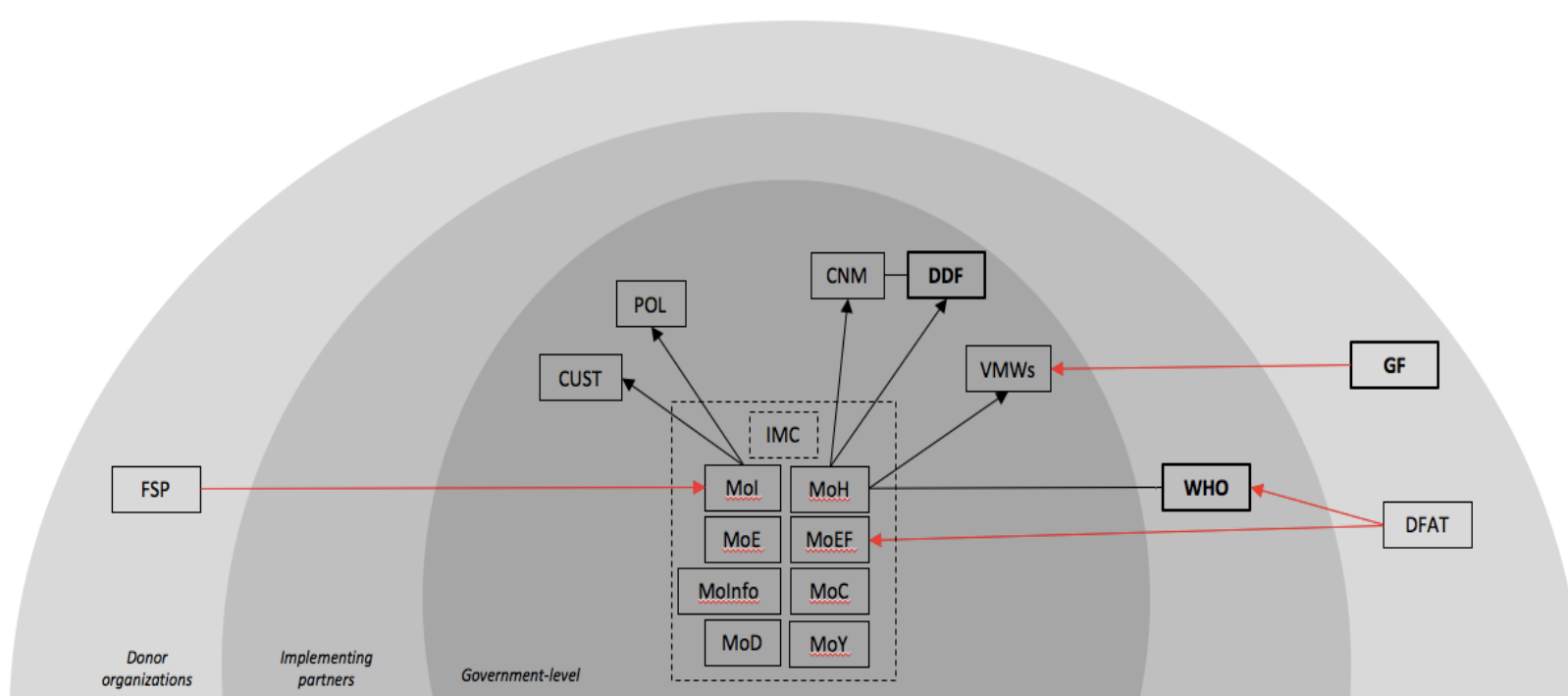
Figure 10 Cambodia Map of Stakeholders

Symbol	Description
→	Funds
→	Supervision / Cooperation
——	Cooperation

Figure 11 Legend for Map of Stakeholders

*The landscape of policy actors represented above is an attempt to visually represent complex and dynamic interactions between several actors, whose professional links are not limited to those represented here. These interactions change over time and this map only captures a snapshot in time to support the reader's understanding of the position of the IMC.

6.2.2.2   A focus on artemisinin resistance and oAMTs

Following the establishment of the IMC, the main focusing event in line with this second phase has been the increasing evidence of artemisinin resistance at the Thai-Cambodian border. This marked a phase of capacity building for efforts against substandard medicines in particular, by streamlining the distribution of ACTs and reducing access to banned oAMTs. The Good Pharmacy Practices Guide (2006), for example, has a specific section on AMLs, specifying that the sale of oAMTs is prohibited, that diagnostics should be performed first, and that serious cases should be referred to closest public health service. This provides instructions on the sale of pharmaceutical products from labelling instructions to adequate warehousing and storage facilities. It also discusses how to deal with 'spurious' or 'expired' medicines – to be kept separately for destruction. It does not, however, define what constitutes a 'spurious' medicine. By 2007, the WHO had banned the use and production of oAMTs and the Cambodian government followed suit in 2008, by officially banning the use, production and sale of oAMTs in Cambodia.

6.2.2.3   Revised legal framework for pharmacovigilance

Fears regarding the spread of artemisinin resistance and the ban on oAMTs coincided with a second window for pharmaceutical policy change and the introduction of the 2007 Amendment to the 1996 Law. The problem of poor-quality medicines was first mentioned in the Law on Management of Pharmaceuticals (1996). Article 12 of this law defined the scope of a penalty for medicines that are 'counterfeit' or of 'non-quality', as well as for 'expired' or 'unauthorized' medicines. Here, the definition of poor-quality medicines revolved predominantly around trademark infringement and non-registration. The falsification of pharmaceutical products was addressed exclusively as a commercial fraud (for example in the Law on the Management of Quality and Safety of Products and Services (2000)) or as a trademark infringement, rather than a crime. The 2007 Amendment clarifies the definition of a 'counterfeit' medicine (Article 2.2), but alludes first and foremost to the substandard nature of the product with a dose of Active Pharmaceutical Ingredient (API) below the required threshold for drug efficacy. This definition does not encompass the notion of 'intent', which would qualify a poor-quality medicine as 'falsified'. Once again, there is an amalgam of definitions between substandard, unregistered/unauthorized/expired, as well as counterfeit medicines. More specifically, the 2007 Amendment emphasizes the importance of addressing Adverse Drug Reactions (ADR) and improving pharmacovigilance (PV), in line with fears of rising resistance. The Amendment granted the MoH a mandate to recall batches in case of

reported ADR. The recall procedure does not refer to terminology of 'falsified' medicines but discusses pharmaceutical products that are 'dangerous to health'. This suggests an emphasis on monitoring ADR rather than addressing the threat of pharmaceutical crime. The Good Pharmacy Practices Guide (2006) highlights the role of pharmaceutical outlets in ADR reporting and product recall. In parallel to this renewed emphasis on PV activities, in 2008 the Cambodian PV centre was established[34] with a Medicines Safety Advisory Committee. Despite the establishment of a PV centre, the electronic reporting database and national pharmacovigilance guidelines were only introduced in 2012 and ADR reporting still remains low – at 3% in 2011 (Nwokike *et al.* 2013).

The 2007 Amendment also introduced changes regarding the penalties incurred for the import, distribution or sale of poor-quality medicines, which suggests a more conciliatory response to such unlawful activities. The 2007 Amendment outlines penalties for the production, import, export, and trade of 'counterfeit drugs', as well as pharmaceuticals of 'non-quality' (at Article 12), and imposes a lower fine[35] than stipulated in the 1996 Royal Kram. Furthermore, the 2007 Amendment reduces the severity of the punishment for accomplices to an 'administrative penalty' instead of a fine (at Article 13). These revisions deter efforts towards a more transparent inspection process and suggest limited political will to penalise activity around counterfeit or non-quality drugs. Instead, the focus of policy efforts appeared to be on containing the threat of artemisinin resistance and enforcing the 2008 ban on oAMTs. The focus shifted away from poor-quality medicines as a pharmaceutical crime towards the challenge of substandard and unregistered medicines (oAMTs in particular), and the risks that these pose for the spread of artemisinin resistant malaria.

6.2.3 Phase III: Strengthening post-marketing surveillance against oAMTs (2010-2016)

6.2.3.1 Enforcing the ban on oAMTs

In the third phase of the policy development process, the introduction of a Medicines Policy (2010) offered a window of opportunity to align the role of the DDF and the MoH with the Health Strategy Plan (2008-2015) and the National Strategic Plan for Elimination of Malaria (2011-2015). As reported by Yeung *et al.* (2011), access to quality subsided malaria commodities in remote areas of Cambodia remained poor. In line with such evidence, the Medicines Policy focuses more specifically on the promotion of equitable access to good

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[34] The PV Centre is housed within the DDF, under the Essential Drugs Bureau.
[35] A fine of 2-10 million Cambodian Riels instead of 20-50 in the 1996 Royal Kram.

quality, safe and efficacious medicines and on promoting the rational use of medicines (including AMLs). It also calls for stronger PV efforts by encouraging health workers to report ADRs more systematically, and by strengthening the national laboratory known as the National Health Products Quality Control Centre (NHQC) to reach international standards, calling for a re-organization of its functions. This policy aims to reinforce quality monitoring activities, more specifically, through the enforcement of the ban on oAMTs. The MoH Control Agents, whose authority falls under the Drug Regulation Bureau of the DDF, have a mandate to seize 'counterfeit medicines' and 'other suspicious exhibits', as stipulated in the (2011) Prakas on Roles and Responsibilities of Control Agent. In 2010, the MoH led a crackdown on unlicensed pharmaceutical outlets to enforce the ban on oAMTs, as well as licensing procedures. This initiative marked a turning point when MoH Control Agents raided several pharmaceutical outlets including informal outlets at the Olympic Market (central market) of Phnom Penh. This initiative led to encouraging results (Yeung *et al.* 2015), including the reduced circulation of unauthorized oAMTs (some of which were of poor-quality) and the closure of numerous unlicensed outlets predominantly in urban zones. According to various respondents, government actors capitalized on this successful initiative, which also received a lot of attention in the media and from the international community.

In this third phase, USP and PQM programs also continued their support of the DDF's quality monitoring efforts for AMLs, and supported the enforcement of the ban on oAMTs. As a result of combined sampling and quality testing activities, 22 tons of falsified medicines were seized and destroyed between December 2010 and January 2011 (Fougeres 2011). Despite the support of technical partners, it appears that the focus of the MoH was predominantly on implementing the ban on oAMTs to strive towards malaria elimination in accordance with donor priorities, rather than strengthening post-marketing surveillance activities altogether. In fact, there is no further record in this third phase of concrete initiatives taken by the IMC since the ban on oAMTs. The FSP Mekong (a French government initiative which ended in 2015) did provide funding to facilitate more cross-sectoral cooperation against falsified medicines – but according to respondents' feedback, this initiative has had limited success beyond the ban on oAMTs. Government officials' focusing on the success of the 2010 crack down for example, diverted attention to the broader issue of poor-quality AMLs, including the pharmaceutical crime of medicines falsification and the illicit trade in falsified drugs.

6.2.3.2 Malaria elimination and the ban on oAMTs

The focus on the ban and the enforcement of licensing procedures, results suggest, may have been motivated by the desire to 'contain' the threat of artemisinin resistance to support malaria elimination efforts. Arguably, the driving principle behind this third phase of the policy process seems to be malaria elimination and efforts against artemisinin resistance. Several donors, such as the Australian Department of Foreign Affairs and Trade (DFAT) and the Bill and Melinda Gates Foundation (BMGF), have provided substantial funding in support of malaria control efforts in Cambodia. As suggested by respondents, the bulk of international aid for health in Cambodia is aimed at malaria control and elimination rather than improving medicine quality per se. Donors' interests are geared towards addressing the threat of artemisinin resistance, through initiatives such as the region-wide Emergency Response to Artemisinin Resistance (ERAR) led by the WHO or the Global Fund's Regional Artemisinin-resistance Initiative (RAI). This may explain the government's focus on the ban on oAMTs, as oAMTs are perceived as directly contributing to artemisinin-resistance.

When discussing the policy process and the key policy actors involved against poor-quality antimalarial medicines in Cambodia, respondents regularly mentioned Village Malaria Workers (VMWs)[36] as having played an important role in the fight against poor-quality medicines, by providing information on health seeking behaviour and promoting the rational use of AMLs. ACT watch and Malaria Consortium were also identified as key organizations providing essential data on AML distribution methods. The mandate of these organizations, however, is towards malaria control rather than directly reducing the prevalence of poor-quality antimalarials – although the latter objective can be acknowledged as part of the former. With increasing media attention and sustained donor support for efforts against artemisinin resistance (and therefore against the circulation of unauthorized, poor-quality oAMTs), the government-level representatives emphasize the success of these operations, failing in return to acknowledge the current weaknesses that remain in the drug regulatory system to address the broader threat of poor-quality medicines.

6.2.3.3 Cross-border cooperation

With regards to cross-border cooperation against poor-quality medicines in this third phase, the Medicines Policy (MoH 2010) does demonstrate Cambodia's willingness to engage with

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[36] VHWs are funded through the United States Agency for International Development (USAID) and managed by Cap-Malaria (Cap-M) and the National Malaria Program (CNM).

ASEAN-wide harmonization efforts. Since March 2010, applications for medicine registrations are made using the ASEAN ACTD and ACTR forms as part of the harmonization of pharmaceutical regulatory procedures in Southeast Asia. While official intentions to cooperate regionally are clearer within official documents of the Ministry of Commerce (such as the 2000 Law on the Management of Quality and Safety of products and Services), which institutionalizes the exchange of information with regional associations and international agencies, the Medicines Policy calls for the facilitation of regional cooperation and for sharing common procedures and experiences among ASEAN member states. Although a less systematic commitment, it is an important one nevertheless which suggests an intention to address a threat that is inherently regional (the threat of artemisinin resistance).

6.3   Perceptions of the problem of poor-quality AMLs

In this section, I present the findings from 17 stakeholder interviews conducted in 2015 in Phnom Penh, with representatives from the government, members of implementing partner organizations, donor organizations, as well as external consultants to the Cambodian health sector. These findings are summarized in Table 11 on page 120. While most participants seemed open to addressing the topic of medicine regulation and the problem of poor-quality medicines, there remained a notable degree of political sensitivity around the topic among government-level representatives, which many non-government interviewees were quick to warn me about.   Some mentioned that this sensitivity might be due to government-linked vested interests in what has been described as a rather opaque procurement process. Due to the political sensitivity, many government officials refused to be interviewed. In some cases, I had to shift the focus of the interviews with some respondents to 'access to medicines' as a general topic before addressing the perceived threat of loosely termed 'poor-quality medicines', including both falsified and substandard medicines. For the Ministry of Interior representatives (in charge of the inspection of medicines for example), a lengthy bureaucratic process to request an interview made it impossible to interview a representative before the end of my fieldwork. Thus, I was only able to interview two government-level respondents in Cambodia. Due to the difficulty of obtaining open accounts regarding the situation of poor-quality medicines, many more interviews were conducted with implementing partner (IP) organizations and International Organizations (IOs) working with the Cambodian Ministry of Health (MoH), and whose views served to provide additional information on the Cambodian situation.

Frame	Description
Medical	Government respondents dismiss the challenge of poor-quality AMLs and emphasize the problem of oAMTs for malaria elimination.
Political	Non government respondents highlight the lack of transparency in policy processes, the supply chain of pharmaceuticals and quality monitoring efforts, linking the problem of vested interests to the low political commitment to the problem of poor-quality medicines.
Regulatory	Both categories of respondents refer to the lack of financial and human capacity and poor cross-sectoral cooperation efforts to regulate pharmaceutical effectively.
Health Systems	Non-government respondents explain that the patchy access to health services and the distribution of cocktails of drugs through unqualified pharmacy personnel, are health system challenges that impact access to quality medicines. Patchy access to health services and lack of enforcement of health practitioner licenses.
Security	Government respondents describe the problem of poor-quality medicines as a problem coming from the region and posing a national security concern, while both categories of respondents stated that the demand for cheaper accessible treatments among MMPs remains a challenge that requires better cross-border cooperation.
Economic	Few references were made to the economic frame, however, respondents expressed concern at the increased flow of illicit goods following the AEC 2015 and discuss the affordability of AML treatments.

Table 11 Summary of frames detailing stakeholder perception of factors contributing to the circulation of poor-quality medicines in Cambodia

6.3.1   Medical Frame

6.3.1.1   Focus on unauthorised medicines

A common viewpoint among government-level respondents including representatives from the DDF, was that poor-quality medicines were 'no longer a problem' in Cambodia, especially since the 2010 crackdown on unlicensed outlets to enforce the ban on oAMTs. Government respondents largely framed the case of Cambodia as a concern for rising artemisinin resistance, and regularly diverted our discussions on falsified and substandard medicines towards risks of substandard or unauthorised medicines including oAMTs for rising resistance to artemisinin. Respondents often placed issues related to unauthorized medicines and poor-quality medicines in the same basket:

> The issue of oAMTs, poor-quality, and substandard, fake medicines and so on, [all] this is a business. (STK08NG_LNGO20150402)

During our interviews, it was common for government officials to steer the discussion away from the topic of falsified medicines and re-centre the debate around oAMTs, as illustrated in this response on poor-quality medicines:

> Until today we have very good results that suggest that […] it's hard to find monotherapies [in] private outlets. But we cannot say zero, we have to assess further if possible. (STK08NG_LNGO20150402)

In a process of frame shifting, respondents shifted the focus of discussions away from the problem of poor-quality medicines and towards unauthorised medicines. Instead, government level respondents alluded to the fact that poor-quality medicines, even if they may be smuggled into Cambodia, 'could not be sold in the country' (STK10G_NMCP20150402); therefore dismissing the existence of unlicensed providers and the informal supply chain, through which these products might reach patients. The respondents interviewed were quick to highlight the success of Cambodia's efforts against unregistered oAMTs as a treatment no longer recommended by the WHO and unauthorised for sale in Cambodia. Government respondents referred to three key initiatives including the IMC in support of the ban on oAMTs, as well as the PPM program, to illustrate Cambodia's efforts against unauthorised medicines.

6.3.1.2 Malaria elimination

Through this process of frame shifting, respondents re-centred the discussion on malaria control efforts, rather than efforts against poor-quality essential medicines in general. The focus on malaria elimination efforts was a common tendency among other non-government respondents. The results suggest consensus among government-level and non-government respondents on the fact that the policy initiatives detailed above have successfully contributed to improving access to quality AMLs. Some respondents shifted the discussions on to the VMWs, arguing that they had been instrumental in preventing patients in hard to reach areas from seeking care from unlicensed outlets. This is yet another example of how respondents framed the issue of poor-quality medicines in terms of malaria elimination.

Most government respondents shifted the focus away from the pharmaceutical crime of falsification to emphasize the success of Cambodia's efforts towards banning unauthorized medicines including oAMTs, in support of efforts towards malaria control and elimination efforts. By shifting the narrative to oAMTs and unauthorized medicines, respondents highlight the importance of malaria control efforts in Cambodia as a key policy priority, rather than efforts against the pharmaceutical crime of medicines falsification. While most government-level respondents refrained from using the terms 'counterfeit' or 'falsified', many refocused our discussions on the issue of 'substandard' medicines, as well as oAMTs. A local staff member from the principal recipient organization for example, clearly steered the discussion away from the topic of 'counterfeit' medicines towards substandard medicines:

> In terms of the word that you used: 'counterfeit' drugs, another word that is also used is 'substandard' drugs. So, this kind of drugs is the link to the word 'resistance' or drug resistance. (STK05NG_IGO20150401)

Local respondents often insisted on the problem of substandard medicines in so far as they have been found to contribute to the problem of artemisinin resistance, perceived as the main public health challenge in Cambodia's border provinces. While shying away from terminology linked to medicine falsification, most respondents used medical language to emphasize the dangers of substandard medicines, talking about 'failure rates' and 'drug efficacy' as a threat to malaria elimination efforts.

6.3.2 Political Frame

There is a discrepancy between the government narrative and that of non-government respondents, as the latter were quick to highlight the political barriers to efforts against poor-

quality medicines, including AMLs. Most non-government respondents' narrative referred to the political frame with three key themes: transparency and corruption; a lack of political will, and the influence of donor organizations on the policy process. Non-government respondents argued that barriers of a political nature hinder the sustainability and ownership of policy efforts against poor-quality medicines including AMLs.

6.3.2.1   Transparency and corruption

The issue of 'transparency' in Cambodian politics, was largely brought to my attention by non-governmental respondents. Under this theme, respondents referred to the wider problem of poor-quality medicines beyond AMLs and beyond malaria control efforts. Non-government-level respondents detailed the lack of transparency in policy processes, the supply chain of pharmaceuticals and quality monitoring efforts, as well as the unreliability of the official data on the circulation of poor-quality medicines in Cambodia. PSI acknowledged that data flow was a challenge in Cambodia, with figures on the prevalence of poor-quality medicines from DDF often being unavailable or kept hidden (STK04NG_INGO20150321). Many respondents suggested that it is indeed difficult to obtain open accounts on issues of access to medicines from government officials, that there is high sensitivity around malaria control efforts and that malaria treatment guidelines in Cambodia are 'a very political matter'. One respondent also referred to the problem of 'pharmaceutical procurement efficiency', insinuating a lack of transparency regarding the MoH budget as a potential driver of the problem of poor-quality medicines (STK06NG_Donor20150401). Other respondents argued that the bidding process for imported medicines was often skewed and that the government would sometimes 'push down' cheaper medicines of compromised quality or shorter shelf life. It was also mentioned that the procurement budget is very tricky to delve into with government representatives, who are aware that it could uncover unfair practices along the supply chain of pharmaceuticals. Considering the highly sensitive nature of these claims, it was therefore not possible to verify this information with the DDF. No government respondent mentioned the procurement budget or alluded to the report by the GF Office of the Investigator General on allegations of malaria grant mismanagement and the loss of PR status by CNM.

Respondents explained that the lack of transparency and instances of corruption inevitably affect the implementation and effectiveness of existing rules and regulations to prevent the circulation of poor-quality medicines. Additionally, respondents argued that current national penalties against the manufacture, sale and distribution of poor-quality medicines remain too weak to act as a deterrent as the enforcement of existing rules and regulations has been reported

to be uneven across Cambodia. Other non-government respondents added that existing policy efforts against poor-quality AMLs may not be sustained in the long-term, due to vested interests among MoH control agents and law enforcers. One respondent said that, due to their low salaries, enforcement officials tend to seek extra income as wholesalers or suppliers of pharmaceuticals. For example, some control agents from the DDF have been reported to own pharmacies or manufacturing sites. Respondents also indicated that with a vested interest in the industry, some control agents might refrain from enforcing regulatory inspections across the supply chain or from surveying their own manufacturing sites. Respondents alluded to other events that suggest a lack of transparent decision-making within the DDF, including the sudden loss of lease of an internationally operated drug testing facility following the discovery of poor-quality medicine products in Cambodia – requiring costly equipment to be moved from one day to the next.

6.3.2.2   Political will and accountability

Respondents from non-government organizations also argued that the sustainability of existing policy initiatives and the commitment they represent against poor-quality medicines, was challenged by a lack of political will. The common argument was that there was both a lack of will to recognize the problem and to tackle it in the long term, through the regular inspections of drug outlets or through the prosecution of wholesalers and retailers found to distribute poor-quality medicines. It was mentioned that political commitment was more evident at the central level – in Phnom Penh – and more diffuse in the rural areas of the country, mainly because of the lack of accountability mechanisms for health inspectors in rural areas. One respondent added that community mobilization systems would be required to ensure that what is agreed upon in Phnom Penh is applied across all provinces. While most respondents – both from the government and others – agreed that it was ultimately the responsibility of the DDF to tackle the problem of poor-quality medicines, many also argued that multi-sectoral cooperation was necessary to leverage resources and combine expertise for effective policy making against the circulation of poor-quality medicines.

Respondents also referred to power strife among government-level policy actors, as one important dimension of the problem of poor-quality medicines in Cambodia. They argued that efforts to improve access to quality medicines are spearheaded by strong political figures with little accountability. One anonymous non-government respondent stated that:

> The MoH is not one thing, it is a collection of various strong people and they
> have their 'fiefdoms' and they protect it. (STK09NG_LNGO20150402)

The reported lack of synergy within and across departments provides no checks and balances for the effective implementation of regulation of the pharmaceutical supply chain. Other respondents referred to a government-wide political power-strife impeding policy processes within the MoH. One respondent detailed the control of the Ministry of Economy and Finance (MoEF) over the MoH procurement budget, illustrating the case when MoEF had cut the procurement budget by USD 30-40 million to match the amount which was estimated missing from the procurement budget. Issues of power and accountability within the government were described as factors mitigating the success of current policy initiatives and impeding stakeholder cooperation.

6.3.2.3   Donor priorities

Numerous government-level respondents also emphasized the importance of cooperation with implementing partners and international organizations, to support policy making for improving the quality of pharmaceuticals. Despite strong partnerships with USP and PSI, however, many respondents referred to the divergence in health partners' expectations and priorities. The varying mandates of these organizations are dictated first and foremost by donor organizations' funding priorities, as an external health consultant pointed out during our interview:

> There's a danger that a lot of donor funding is driven by external pressure as opposed to demand or need-driven priorities. (STK03NG_Consult20150331)

Some explained that activities for improving access to quality medicines tend to be encompassed within wider yet more tangible objectives, such as malaria elimination or the containment of artemisinin resistance. Respondents explained that the issue of resistance has attracted many donors to Cambodia, resulting in a crowded and a reportedly largely fragmented landscape of initiatives.

6.3.3   Regulatory Frame

Beyond the political frame, issues of policy-making, transparency and cooperation, the narratives from several respondents from non-government organizations predominantly fit within the 'regulatory frame', encompassing issues related to the legal and regulatory frameworks and the implementation of existing policy mechanisms for securing the supply chain of pharmaceuticals.

6.3.3.1 Surveillance and Enforcement capacity

Results show that the rules and regulations stipulated in policy or legal documents are not necessarily enforced on the ground. Most respondents, including some government-level respondents, highlighted a lack of institutional capacity – linked to low financial and human resources within the MoH – leading to a dearth in de facto regulation along the pharmaceutical supply chain. Even the enforcement of the ban on the sale and distribution of oAMTs was more patchy in peripheral rural areas of the country where unlicensed outlets selling oAMTs continue to operate (Khan, Akazawa, *et al.* 2011; Krech *et al.* 2014). A common viewpoint among respondents was that the lack of enforcement of pre-marketing regulations, including the licensing procedures on suppliers or importers for example, presents an added risk for the circulation of poor-quality medicines, as the government fails to address the problem at its source. In practice, one interviewee explained, any overseas manufacturer of generic medicines (from India for example) obtains a license based on a single sample batch of 'good quality' products, while subsequent batches are no longer quality-checked, therefore leaving room for poor-quality medicines to infiltrate the market. While the Medicines Policy (2010) encourages manufacturers to obtain GMP certification, respondents maintain that this requirement is not enforced as manufacturers are issued licenses to produce medicines regardless. Studies suggest a high rate of non-compliance with rules and regulations among wholesalers and distributors. One study in particular, suggests that only 10% of wholesalers interviewed had an up-to-date license to produce medicines (Yeung *et al*. 2011). For AMLs, DDF reportedly requires AML manufacturers to be both GMP certified and WHO pre-qualified. In practice, however, respondents reported that due to the lack of WHO-prequalified suppliers for certain ACTs, CNM has reportedly procured antimalarials from non-WHO prequalified manufacturers, with pre-approval from the GF.

Respondents explained that many pharmacies operate without a license, and fall beyond the regulation mandate of the DDF. Some mentioned the high number of requirements on licensed outlets, insinuating that this might dissuade drug vendors from obtaining or renewing their licenses. A major weakness in efforts to regulate the supply chain of medicines, according to a respondent from PSI, is that the private and public sector outlets are not addressed collectively:

> You either look at just the private sector or the public sector, but it's very rare
> that both of these things are being viewed collectively.
> (STK04NG_INGO20150321)

Respondents also perceived post-marketing surveillance and quality monitoring activities as being inefficient and irregular. To illustrate this argument, some respondents also mentioned a general lack of capacity for quality monitoring activities. They reported that control agents with the mandate to conduct these operations are stretched out too thin, their mandate including a wide scope of responsibilities ranging from enforcement of manufacturing regulation, import and export rules, as well as the opening / closing of pharmacies. As stipulated in Prakas on Roles and Responsibilities of Control Agents (2011), control agents are also in charge of food and hygiene issues. Respondents also mentioned the GF's parallel post-marketing surveillance system for AMLs, arguing that without GF budget, the government does not conduct sampling procedures to an acceptable standard. As another example, respondents from implementing organizations point out that efforts to close down unlicensed pharmaceutical outlets in 2010, may have been a one-off albeit successful effort, but that it remains unclear whether the control agents conducted operations of this scale since 2010:

> There have been statements about […] clamping down on pharmacies that don't have an actual pharmacist sitting behind the desk. It rarely seems to turn into more than just one action […] it is not a systematic thing. But when something real happens which is international news - suddenly local doctors are on the run. (STK09NG_LNGO20150402)

Respondents added that the current pharmaceutical regulatory system needs to be strengthened and requires a more proactive, rather than a predominantly reactive, approach to regulation. Numerous interviewees cited the incident in the Roka commune of Battambang Province where, in December 2015, an unlicensed village doctor inadvertently infected 200-300 patients with HIV/AIDS through intravenous treatments, due to poor medical practice. Triggered by the international media attention around this incident, the government took a strong stance against unlicensed practitioners, using this incident as a political showcase of their regulatory authority. As respondents pointed out, this is hardly evidence of systematically applied regulatory practice, but instead a 'crisis driven theory of change' (STK09NG_LNGO20150402).

Other respondents explained the lack of capacity to implement thorough and systematic pharmacovigilance operations. While DDF is currently training to improve their reporting capabilities, pharmacovigilance reporting on adverse drug reactions remains very sporadic partly due, once again, to a shortage in human and financial resources. As indicated from the policy documents, this is not surprising considering there is no dedicated budget for

pharmacovigilance activities. Another illustration of this lack of capacity relates to the national laboratory, which is said to lack the necessary equipment and is largely understaffed:

> They [the laboratory] are under-resourced, under-funded and I think there's only two or three people there. (STK03NG_Consult20150331)

Because of the low capacity of the national laboratory, it is not able to test the quality of AMLs. The GF sends ACT samples for quality testing to an ISO-accredited laboratory in Nepal. The national laboratory is currently in a capacity building phase, with funding support from the United States Agency for International Development (USAID) and the World Bank, and with technical assistance by USP. The lab is to be ISO Certified and WHO-prequalified in the near future, although another respondent stated that this process has been dragging on over the years and it is unsure when it will be completed. While standard operating procedures are in place, weak technical capacity impedes the DDF's ability to adequately monitor the quality of medicines.

Another reason given for the lack of post-marketing surveillance is the relatively low salaries of MoH control agents. One respondent explains that in most countries, 75-80% of the MoH budget is typically dedicated to staff salaries. This figure is only about 45-55% in LICs. However, in the case of Cambodia the proportion of the budget reserved for staff salaries is 18-20%, which indicates a proportionally low salary for law enforcers within the MoH (and a comparatively high budget for procurement representing over 50% of the total budget). Control Agents are therefore not incentivized to monitor the quality of services and products effectively. Respondents added that the large scope of their quality monitoring tasks across numerous outlets throughout the country is overwhelming, and that there are not enough agents or trained police officers to collect information, to report or to monitor the situation regularly.

Respondents pointed to both the lack of policy enforcement, as well as the low prosecution rates for anyone involved in the circulation of poor-quality medicines, as reasons why the problem persists. One respondent explained that cases rarely make it to court, and that those sanctioned for pharmaceutical crimes are more likely to be the manufacturers or the smugglers rather than the producers themselves, suggesting that the existing laws are skewed in their scarce implementation and fail to address the problem of medicine falsification effectively. Finally, the regulatory frame, as one of the main frames in the narratives of interviewed respondents, explains why, because of the lack of capacity within the government to enforce

existing policy and legal mechanisms, multi-sectoral and stakeholder cooperation is a key prerequisite to harness the expertise and resources of each towards securing the supply chain.

6.3.3.2 Lack of stakeholder cooperation

Some non-government respondents reported that there is no synergy across functions within the MoH, and that most operations are spearheaded by strong political figures who use information to their advantage, and are reluctant to share the results of their activities with other parts of the ministry – therefore impeding on enforcement efforts. Government-level respondents (while generally dismissing it as problem in Cambodia) agreed that the global problem of poor-quality drugs goes beyond health and requires the involvement of customs, policy, justice departments – and highlighted the value of the IMC in this respect. Most government respondents referred to the IMC as the key initiative in Cambodia, harnessing cross-ministerial cooperation against poor-quality medicines. Regarding the enforcement of the ban on oAMTs, most respondents agreed that the 2010 crackdown on unlicensed pharmacy outlets had a positive impact on improving access to quality AMLs. Since then, respondents acknowledged that the number of unlicensed outlets had considerably reduced. The common viewpoint was that the confiscation of stocks deemed of poor-quality, is indeed not possible without the preliminary intervention of police officials – thereby acknowledging a shared responsibility across the government for enforcing regulations to improve access to quality medicines. Nevertheless, respondents did report that the IMC meetings are irregular and that there have been few common operations since the nationwide implementation of the ban on oAMTs, as briefly mentioned in phase three of the policy process. This, respondents argued, may be due to a lack of political will to address a sensitive topic and a lack of funds to support further joint activities. Other respondents emphasized the need for sustained partnerships for health systems strengthening and access to medicines, beyond one-off mediatized efforts, such as the work of the Control Agents in 2010 in Cambodia or even INTERPOL-led Operations Storm. While these have had a notable impact and successfully led to the closure of illegal drug outlets in Cambodia and beyond, long-term initiatives with strong partnerships across borders are still lacking as a necessary way forward to improve access to quality medicines.

6.3.4   Health Systems Frame

The other predominant frame emerging from the discourses of non-government respondents primarily and some government-level respondents, is the Health Systems Frame. Here, respondents mentioned the weak health services in Cambodia and the impact this has on access

to quality medicines in general, and indirectly, on the circulation of poor-quality medicines including AMLs.

6.3.4.1 Access to medicines

Most non-government respondents referred to the overall structure of the public health care system, the patchy access to services, lack of enforcement of health practitioner licenses and the repercussions this has on access to quality AMLs and other essential medicines. While health insurance schemes, such as the health equity fund, are gradually reaching the population in the aim of improving universal health coverage, access to adequate health care remains a practical as well as financial issue in Cambodia. The fact that expenditure for medicines is mainly out-of-pocket explains why there might be a demand for cheaper alternatives. Historically, the aftermath of the Khmer rouge regime left very few qualified doctors in the public health sector. Since then, many perceive the private sector as being a more reliable and more efficient health care provider. One anonymous respondent working for an international organisation in Phnom Penh, mentioned that most public health facilities are dysfunctional or lack the necessary commodities, sometimes due to poor stock management of medicines:

> If there are facilities there [..] they're not functional or if they are functional,
> there are no commodities, that is a problem. If it [the medicines] is there but it's
> not the right one or it is out of stock, that is also a problem.
> (STK11NG_IGO20150403)

In the most remote areas of the country, the only public health service available for the management of uncomplicated malaria is from health volunteers (also known as 'village malaria workers'), who received basic training and are not certified health practitioners. Other non-government respondents added that health staff in the public sector are generally underpaid, and that the majority resort to dual careers in both public sector and private sector practices to earn extra income. This leads to a shortage of full-time qualified human resources in the public health sector, pushing patients to seek treatment in private sector outlets, including unlicensed ones. Respondents therefore linked weak public health services to general lack of trust among patients towards the system, explaining consumer behaviour and preferences to seek cheaper medicines from alternative sources among patients in the rural areas of Cambodia. The lack of access to quality public health services they reported, also has implications for access to quality subsidized essential medicines (including AMLs), as patients resort to private pharmacies, including unlicensed drug outlets, for diagnoses and treatment.

Respondents emphasized the need to strengthen the health system at large to improve access to health and medicines for all.

6.3.4.2 Opaque procurement of medicines

Numerous non-government-level participants referred to the patchy procurement process as another reason why poor-quality medicines may find their way into the market. Despite the structures for registration being in place, a recent USAID report suggests that 30% of medicines sampled on the market in Cambodia remain unregistered (Nwokike *et al.* 2013). Additionally, information on product registration outcomes are not available online. One respondent working hand in hand with the MoH, explained that the logistics management information system (LMIS) for the procurement of medicines was 'leaky and un-transparent, in need of an overhaul', and that procurement budget figures rarely added up – suggesting that the funds allocated to the procurement of medicines were not used efficiently (STK06NG_Donor20150401). The same respondent added that stock-outs and shortages of medicines remain despite the procurement budget having tripled over the last ten years. It was also reported that the complexity of treatment recommendations also affects the supply of quality AMLs. The treatment guidelines for malaria in Cambodia change regularly to adapt to the changing efficacy rates of treatment combinations for parasite clearance, and to mitigate the risks of artemisinin resistance. One informant at PSI explained that five provinces in Cambodia have recently changed to Artesunate Mefloquine, because DH Priperaquine was losing its efficacy. The same informant added that this complicates their task of distributing commodities nationally, especially when newly recommended treatments are not always immediately registered by the DDF. Respondents also reported that this change of recommendations generates confusion as to which commodities are authorized, and there is a clear gap in the availability of training to keep all distribution outlets up to speed on these changes. They added that it becomes tricky for drug vendors, as well as patients, to know whether the product they are buying from the private sector are authorized, recommended, or even of good quality – as falsifiers might exploit this complexity to create a market for their products.

6.3.4.3 Distribution practices and unlicensed outlets

The third theme under the health systems frame, relates to the proliferation of unlicensed drug outlets and dangerous distribution practices, as reported by both government and non-government respondents. Respondents mentioned that a health care delivery system that

functions inconsistently, has inevitable repercussions on the continuous supply of quality assured medicines through the legitimate supply, leaving a demand for the recommended medicines that is not being fulfilled by legitimate suppliers. This is particularly true, they added, in remote areas where accessibility to the right services is a challenge. For these reasons it was reported that unlicensed outlets, with unqualified staff and inappropriate storage infrastructure, are more common in these areas despite the 2010 crackdown. This adds to the chaotic nature of the private informal drug supply chain or what one respondent referred to as 'pharmaceutical anarchy'. In fact, some government respondents avoided the topic of unlicensed outlets altogether, and re-centred our discussions on the quality monitoring activities of the government in the legitimate supply chain, suggesting that unlicensed private sector outlets fell beyond the mandate and responsibility of the DDF. Other respondents added that poverty in rural areas often comes hand in hand with a lack of education and awareness about the risks of purchasing medicines from unlicensed outlets. Some may be unaware of the existence of VMWs in villages, preferring to purchase their treatments from a familiar vendor who may offer a wider choice of medicines.

Adding to the complexity of the supply chain and patchy procurement of essential medicines, the way that medicines are dispensed and distributed (especially in unlicensed outlets), has been identified by most respondents as another risk factor increasing the likelihood of poor-quality medicines reaching patients. While guidelines for the dispensing of medicines exist (See the Good Pharmacy Practices Guide 2006), many respondents alluded to ad-hoc distribution methods as a risk factor for the circulation of poor-quality medicines. Even in licensed establishments, respondents added, the person selling the medicines is not always a registered pharmacist. In some cases, pharmacies are run by either a family member or friend of the registered pharmacist, doctor or nurse owning the shop. Unqualified personnel may be less weary of the risks of purchasing medicines from unlicensed wholesalers or itinerant drug sellers. Cambodian pharmacists traditionally provide a diagnosis based on the patient's symptoms, and dispense medicines without packaging as a 'cocktail' of pills in a plastic bag referred to as '*Tnam Psom*'. This 'cocktail' may include vitamin C or paracetamol for the least harmless, but also different types of antibiotics without issuing the correct dosage recommendations. Drug sellers in the central market of Phnom Penh ten years ago, a respondent added, would ask the patient whether they preferred the more expensive or cheaper alternative, and would prepare a concoction accordingly using medicines from various knowingly untrustworthy sources, potentially falsified, and obtained at a cheaper price. Other respondents noted that essential medicines including antibiotics and AMLs, can still be purchased without a prescription in both licensed and unlicensed outlets across the country.

6.3.5 Security Frame

6.3.5.1 A cross-border threat

Many government-level respondents perceived the problem of poor-quality medicines as a regional threat – a phenomenon reaching Cambodia from neighbouring countries along the Mekong region – suggesting that, if those countries strengthened their efforts against the circulation in poor-quality medicines, these medicines would never reach Cambodia.

> When you talk about fake or poor-quality medicines it is no longer country specific. This is a push and pull mechanism - if you have law enforcement in one country […] bad medicines will go to the border areas and cross the border -and that is a problem. (STK08NG_LNGO20150402)

This frame links back to the 'success story', whereby government respondents dismissed poor-quality medicines as a Cambodian problem, and tended to shift the blame to neighbouring countries for allowing such medicines to circulate across borders. A respondent from an implementing partner organization stated:

> It's not Cambodia -its regional - if the neighbour[s] could manage strictly their drugs it could be better. (STK05NG_IGO20150401)

Some respondents referred to the geographic proximity of Cambodia to areas known for their production of falsified medicine such as South-western China, or Vietnam – as stated by a respondent from the DDF below:

> In Cambodia, there are also some neighbour countries that import substandard or counterfeit drugs - for example some other drugs from Vietnam - and also from China. (STK05NG_IGO20150401)

Another respondent added that poor-quality medicines might also flow in from Myanmar, where it is implied that the ban on oAMTs has not been successfully enforced yet and regulatory efforts for access to quality medicines in general are lagging behind. The recent establishment of the ASEAN Economic Community (AEC) only exacerbates fears of poor-quality medicines entering the country, through more porous borders and a more significant influx of goods and people into Cambodia. Many respondents also reported that the cross-border circulation of poor-quality and unauthorized medicines is particularly dangerous for Cambodia because of the risks of increased artemisinin resistance. Once again, the 'security frame' bridges to the 'medical frame', with an emphasis on the risks of resistance.

6.3.5.2   Dynamics of migration

Government-level respondents stated that the intense cross-border movement of Mobile Migrant Populations (MMPs) in Cambodia's border areas, poses risks for national security due to the risks of smuggling in poor-quality products, including medicines. Bridging onto the 'medical frame' once again, many added that this is an additional challenge for malaria control efforts.

> …[T]hey [MMPs] bring malaria from the side where they work or they bring malaria from their original country. You see the dynamic of spreading, particularly in terms of artemisinin resistance... and of course it has an impact on malaria elimination. (STK08NG_LNGO20150402)

Cambodia is both a receiver country of migrants from Vietnam and Lao PDR and a sender country, with Cambodians travelling to Thailand for higher paid work. Illegal logging was a major activity at Cambodia's borders in the 1990s but has now reduced. Nevertheless, the flow of migrants persists for other development projects in the area and the movement of seasonal workers is hard to track, as they follow plantations or mining projects. For fear of losing their temporary resident status, or due to their undocumented statuses, respondents reported that migrants are reluctant to seek treatment from public health services in Cambodia. Many therefore chose to self-medicate. Respondents added that migrants drive the demand for medicines from unlicensed vendors such as itinerant drug sellers, and contribute to the circulation of poor-quality medicines by bringing their own medicines from potentially dubious sources into the country, and sharing those with fellow migrant workers.

> [T]he people in this region, when they move around they cross the borders, they tend to keep some medicines with them, and those medicines they purchase from the private sector – that's connecting very well to the quality or to whether it is the right medicine. (STK08NG_LNGO20150402)

Respondents also mentioned a reluctance among migrant workers to seek free AMLs from public facilities, driving an irrational use of medicines and inciting migrant workers to also bring their own doctors. A health consultant based in Phnom Penh commented on the case of Vietnamese plantations along the border:

> They [Vietnamese plantation owners in Cambodia] bring in a doctor and they also bring their own drugs [to the plantations] – that is where we see a lot of the importation of substandard commodities. (STK04NG_INGO20150321)

MMPs bring in services and products that they might feel more familiar with but that escape the control of the DDF, thereby complicating the landscape of drug circulation. Policy actors in Cambodia acknowledged the threat that uncontrolled cross-border movement poses in regards to accessing quality antimalarial treatments, and agreed that migration representatives should be an integral part of both a national malaria program and discussions on how to reduce resistance, as well the circulation of unauthorized or poor-quality antimalarials.

6.3.5.3   Importance of cross-border cooperation

Taking into consideration the scale of this perceived regional challenge, both government and non-government respondents agreed that the challenge cannot be addressed without inter-sectoral as well as cross-border cooperation and leveraging of expertise and resources. Some respondents mentioned current efforts to acknowledge MMP movements across borders, such as Cap Malaria's twin city project and VMWs recruited among migrants working in plantations by PSI, to share information about the risks of poor-quality AMLs and to improve access to good quality treatments. Besides efforts to reach out to MMPs through the VMWs, some respondents emphasized the relevance of fostering regional cooperation by working through supra-national bodies or associations such as ASEAN or the Asia Pacific Leaders Malaria Alliance (APLMA), to coordinate efforts against poor-quality medicines. Both government and non-governments respondents expressed scepticism towards regional harmonization efforts, however, considering the differences in required malaria treatments across the region and the complexity this brings, and the fact that malaria control in Cambodia is a sensitive case due to the risks of resistance. Bridging with the 'medical frame', government respondents reiterated that Mekong countries have different malaria profiles and are at different stages of malaria elimination, making cooperation on the issue of antimalarial treatments challenging. Additionally, some respondents added that ASEAN's role would be limited to fostering dialogue between countries, but the issue of poor-quality medicines was first and foremost the responsibility of the national NRAs.

> Regional bodies help dialogue and cooperation but it is not their responsibility. (STK02NG_INGO20150331)

On the other hand, others spoke of regional harmonization as an essential step and alluded to the role of regional bodies such as ASEAN to spearhead this movement further, while maintaining that governments hold first responsibility to improve medicine quality.

6.3.6   Economic Frame

Respondents in Cambodia scarcely alluded to themes under the economic frame. Although, the ASEAN economic integration process and the ASEAN Economic Community was perceived as an added challenge to monitoring the circulation of illicit products flowing from across Cambodia's borders – including poor-quality medicines.

> ASEAN harmonization will only benefit the rich countries and Cambodia still needs to catch up. (STK02NG_INGO20150331)

Other respondents alluded to the affordability of medicines. Many asserted that because antimalarial treatments are available free of charge from public sector outlets, there is no demand for cheaper antimalarial treatments. Such statements support those made under the medical frame; that poor-quality AMLs were not considered a major concern in Cambodia.

> There are no fake antimalarials because the ones available in the public health sector are heavily subsidized by the Global Fund, therefore there is no incentive for patients to get 'cheaper' medicines. (STK10G_NMCP20150402)

> Fakes are no longer an issue because the treatments are less expensive. Other medicines are still an issue though such as lifestyle medicines also antibiotics. (STK05NG_IGO20150401)

6.4   Frames and the policy process

A few observations can be made about the implications of my findings for policy development in Cambodia. Firstly, both government and non-government respondents mention under the 'Regulatory Frame', that despite many official laws and policies being introduced since 1996 to strengthen the supply chain of pharmaceuticals, there remain gaps in the pharmaceutical regulatory framework, especially with regards to effective enforcement of these rules and regulations. The main reason put forth for this lack of enforcement is the stretched capacity – both human and financial - within the MoH. This lack of regulation, it is implied, may lead to exploitable gaps in the supply chain, driving the demand for medicines beyond the legitimate supply chain and heightening the risks of both substandard and falsified AMLs from reaching patients. Results suggest that most regulatory efforts have been in response to key focusing events – the initial evidence of poor-quality essential medicines, evidence of artemisinin resistance or media attention around a crisis linked to poor-quality health services in the Roka commune. Initiatives for systematic cooperation against poor-quality medicines, such as the IMC, have not been upheld over the long-term. Instead, government officials emphasize the success of one-off enforcement initiatives, such as the 2010 enforcement of the ban on oAMTs and crackdown on unlicensed pharmacy outlets. This shift of emphasis on unauthorised medicines suggests a lack of political interest towards the challenge of poor-quality medicines per se, and seems commensurate with the focus, from 2010 onwards, on less targeted efforts against falsified medicines and a stronger emphasis on efforts against oAMTs.

Both government and non-government respondents framed the issue of poor-quality medicines as a security concern, especially with regards to rising artemisinin resistance at the Thai-Cambodian border. Under the 'Security Frame', both categories of respondents concurred that the flow of MMPs across Cambodia's borders contributes to the challenge of poor-quality medicines. The emphasis on migration and artemisinin resistance as a regional security threat, reflects the government's emphasis on the role of the PPM scheme and the VMWs – to reach out to plantations and migrant workers and work to extend access to quality AMLs for these communities at risk. The geographical position of Cambodia as a hub for border development projects but also as the epicentre of artemisinin resistance, may therefore have shaped the priorities of the government, whose emphasis has been first and foremost on reducing resistance and working to control malaria in border areas. Government representatives argued that poor-quality medicines including AMLs are a greater problem in neighbouring countries, and that these may enter Cambodian borders only through MMPs, thereby shifting the blame for the circulation of poor-quality medicines away from the government. While both categories of respondents recognized the regional threat that the circulation of poor-quality medicines

represents, there was a notable reluctance among respondents regarding the feasibility of cross-border efforts. Once again, government representatives expressed scepticism towards the role of supra-national bodies such as ASEAN but praised instead, the ground-level initiatives with cross-border ties such as the VMW and the PPM initiative. As the government respondents interviewed also represent Cambodia in international for a, such as the ASEAN Pharmaceutical Product Working Group, this scepticism could explain the lack of emphasis towards regional harmonization of efforts for the regulation of medicines.

Among government respondents, the problem of poor-quality medicines was framed more as a medical concern. It was not framed as a criminal law issue, and the language used is predominantly clinical rather than legal. The 'Medical Frame' was the dominant frame among government-level policy actors interviewed, within which respondents refocused the issue of poor-quality medicines on the associated risks of artemisinin resistance and the need to strengthen efforts towards malaria elimination. This frame shift could be explained by the priorities set by the mandates of key donor organizations. Donor organizations may also emphasize technical approaches to dealing with poor-quality medicines, artemisinin resistance and to working towards malaria elimination, while avoiding the politically sensitive issue of poor-quality medicines. A common viewpoint among respondents was that Cambodia was a 'step ahead' of its neighbours in terms of malaria control efforts. Focusing on artemisinin resistance and malaria elimination, however, does not bode well for the case of other therapeutic categories of potentially poor-quality medicines that may be circulating in the country, and for general efforts to improve access to quality medicines.

Under the medical frame, government respondents also denied the problem of poor-quality medicines as a 'Cambodian problem', and shifted the responsibility for the issue to neighbouring nations and to the movement of migrant workers. Most government respondents deviated from the debate around 'falsified', 'fake' or 'counterfeit medicines', and re-centred the discussions around the problem of 'substandard' or 'unauthorized' medicines. The fact that 'falsified' was not a part of the local respondent's discourse is not surprising in so far as it is not part of official definitions either. Instead, many respondents focused on 'drug efficacy', once again mirroring the main frame that emanate from the primary law and policies focused on the regulation of pharmaceuticals. Both in the legal documents available as well as in the discourse of government-level respondents, there tends to be an amalgam of definitions between falsified, substandard and unauthorized medicines. This amalgam of definitions is problematic, since these categories require distinct policy solutions and legal sanctions.

Non-government respondents, while validating the success of Cambodia's efforts to enforce the ban on oAMTS, discussed the lack of transparency and corruption to explain that the official discourse should be interpreted with caution. Under the 'political frame', however, non-government respondents argued that the reported successes against poor-quality medicines, although validated by some recent evidence of lower rates of poor-quality oAMTs, might also be explained by a lack of transparency on data held by the DDF regarding the quality of other types of medicines. Non-government respondents emphasized that the sensitivity around the issue of poor-quality medicines means that some government officials were not willing to address the topic. This resonates with an apparent lack of political will to target the problem of poor-quality medicines especially the pharmaceutical crime of falsified medicines, as well as with the 2010 policy shift towards improving pharmacovigilance, drug efficacy rates and adverse drug reactions reporting; rather than focusing on cross-sectoral cooperation against the potential production, smuggling and distribution of criminally produced poor-quality medicines. Instances of corruption, especially with regards to the procurement budget, or in the form of vested interests in the pharmaceutical industry, respondents argued, still pose a problem for accessing quality medicines in general. The arguments put forth under the political frame seem commensurate with the shift incurred by the 2007 Amendment towards lighter penalties for the circulation of poor-quality medicines and, in particular, for officials acting as accomplices in such activities.

Non-government respondents also explained that weak enforcement of current regulations and political strife has an impact on the health system in general. Under the Health Systems Frame, they argued for the need to improve access to medicines through health systems strengthening and good governance. Non-government respondents pointed out that because of Cambodia's tumultuous political past, the public health sector has been largely weakened. As a result, the private sector is still perceived among patients as a more trustworthy alternative. Government respondents agreed that the proliferation of unlicensed drug outlets is a challenge that only complicates the overall supply chain of medicines. This seems to correspond with the importance granted by government officials to the 2010 enforcement on the ban on oAMTs and the successful closure of unlicensed outlets. In the process of developing laws against the circulation of poor-quality AMLs, respondents alluded to the government's intention to ban the sale of AMLs from the private sector altogether. This was presented as a source of policy controversy among policy makers, with some arguing that such a decision would impact access to medicines altogether, since a large proportion of the population still relies on the private sector for access to health and medicines. In this sense, respondents recognized the need to further incorporate the private sector under the regulation of the DDF to improve

access to quality AMLs, which is the purpose of the PPM program. The PPM program and PSI's branded medicines were framed as an important initiative to improve access to quality AMLs through the licensed private sector – where most patients in Cambodia still seek treatment. The majority of respondents concurred that the patchy supply and distribution of pharmaceuticals and weak enforcement capacity (especially at the provincial level) of pharmaceutical regulations, still represent a challenge for access to essential medicines in general. Ultimately, non-government respondents conveyed that, while the availability of poor-quality antimalarials may indeed have reduced considerably since 2010, the problem is likely to persist for other substandard or falsified essential medicines.

Recent studies suggest that the presence of poor-quality medicines and especially of oAMTs has considerably reduced since 2010. However, poor-quality medicines in general remain a problem in Cambodia. Krech and colleagues (2014) report that failure rates have fallen from 7.4% in 2006 to 0.7 in 2011, but that poor-quality essential medicines can nevertheless still be found. Falsified lifesaving medicines like antibiotics are still found in community drug outlets, grocery stores, village shops as well as open markets (Khan, Okumura, et al. 2011; Yoshida et al. 2014; Krech et al. 2014; Lon et al. 2006; Phanouvong, Raymond, Krech, Dijiba, et al. 2013; ACTwatch Group & PSK 2014). The literature suggests that the supposed source of these poor-quality medicines lies in India, China or Thailand, labelled with names of (often bogus) companies such as VKP Pharmaceutical Co (Thailand), Brainy Pharmaceuticals or Guilin Pharmaceuticals (China) (Krech *et al.* 2014). Gaps remain therefore in Cambodia's drug regulatory framework to address the threat of poor-quality medicines.

Chapter 7   Laos Results

7.1   Introduction

Figure 12 Map of the Lao People's Democratic Republic (Source: United Nations; available at www.un.org)

Laos, officially known as the Lao People's Democratic Republic (Lao PDR), is a socialist republic with a President, Prime Minister and Ministers forming the main executive body, and a National Assembly as a legislative body (WHO 2011). Laos is a land-locked country which borders five other Mekong countries (see Figure 12): China to the north; Cambodia to the south; Thailand to the west with a long border of 1,800km; and Vietnam to the east with a 2,000km border. Laos shares a small part of its north-western border with Myanmar, at a location commonly referred to as the 'Golden Triangle'. Due to its long borders, Laos is known as a transit country for the circulation of goods and people in the region (Kerr *et al.* 2012; Stuart-fox 2006). Forest covers over 45% of a landscape which is predominantly mountainous, especially in the northern parts of the country. The Mekong River runs along the western border of Laos, with many rivers and streams flowing through the land, making Laos a target country for investments in hydroelectric power generation. Laos is also rich in natural resources such as iron, coal, zinc, copper, gold, and silver. The 6.8 million population of Laos

is diverse and predominantly rural, comprising of 49 ethnic groups. Ethnic Lao people represent just over half of the population (WHO & MoH Lao PDR 2012).

Laos has had a tumultuous history with long periods of colonization throughout the 19th and 20th centuries. The country was under French colonial rule from 1893-1953. The legacy of French colonialism for the health sector was minimal, as the system in place at the time catered mainly for the expats and the ruling elite (Stuart-Fox 1997). Soon after the end of the First Indochina War, and the Geneva Conference of 1954, Laos was drawn into further conflicts, including the Second Indochina War and Civil War between two factions – the royalists and the communist 'Pathet Lao' (Meessen *et al.* 2008). During the Vietnam War, from 1963 to 1973, the north-eastern part of Laos was heavily bombed (Boupha 1997). The monarchy was subsequently defeated, resulting in the end of the Kingdom of Laos, and the establishment of the Lao People's Democratic Republic in 1975 (UNDP 2016), with the first constitution signed in 1991. Laos is divided into 18 provinces, including the Nakhon Luang Viangchan Prefecture with Vientiane as its capital. As a single-party socialist country, Laos is governed predominantly by decrees. Since the establishment of the Republic, Laos has gone through various periods of de-centralization and re-centralization (Kongsap *et al.* 2014). The government is now working to further develop a de-centralized health-care system by strengthening district-level management, planning and budgeting in order to overcome difficulties, including the lack financial resources to train provincial level staff (Phommasack *et al.* 2016; Kongsap *et al.* 2014).

Indicator	Value	Year (Source)
Total Population (million)	6.8	2015 (WB)
Gross Domestic Product – per capita Purchasing Power Parity (International $)	5,675	2015 (WB)
Human Development Index (HDI)	0.575 (Rank 141)	2015 (UNDP)

Table 12 Laos economic and development indicators

Laos is a member of ASEAN since 1997 and a member of the WHO Western Pacific Region Office. It has been classified within the Lower-Middle Income Country (LMIC) income category of the World Bank (WB) since 2011, and has benefited from steady GDP growth of 7% over the last ten years (WB 2016). Laos switched from a centrally planned to a market-oriented economy in 1986 (Kyophilavong *et al.* 2014), and infrastructure developments including better regional road networks –referred to as 'economic corridors' – have increased

the connectivity between Laos and neighbouring countries and boosted trade (WHO & MoH Lao PDR 2012). The economy is driven predominantly by the agricultural sector, which employs up to 80% of the Lao workforce and represents a third of the GDP (Kongsap *et al.* 2014). Laos has long been a large producer of opium, although there have been successful efforts to replace opium fields with crops and to reduce addiction to the drug in the country (WHO 2011). The rest of the economy is driven predominantly by foreign direct investment in natural resource extraction including mining, deforestation for timber and pulp, and in the generation of hydro-electric power (WHO and MoH Lao PDR 2012). While overall poverty has reduced in Laos, 23.2% of the population still live below the poverty line according to the Asian Development Bank (ADB 2014). Poverty primarily affects the remote highland areas and is linked to poor road infrastructure (Kongsap *et al.* 2014). One main challenge to the economic development of Laos, highlighted in the literature, is a reported lack of mechanisms for accountability in policy making and implementation. The literature suggests that that there is room for improvement in the transparency of operations for customs control and for the collection of taxes (Stuart-fox 2006; World Health Organization 2011c).

7.1.1   The Lao health sector

Indicator	Value	Year (Source)
Total Health Expenditure (% of GDP)	1.9	2014 (WB)
Heath expenditure per capita (current US$)	33	2014 (WB)
Out-of-Pocket Health Expenditure (% of Total Health Expenditure)	39	2014 (WB)
Physicians per 1000 population	0.27	2010 (WB)
Life expectancy	66.1	2014 (WB)

Table 13 Laos health indicators

The division of Laos during the war led to the creation of two zones with different health systems, which lasted until 1975: a communist led 'Pathet Lao' with military hospitals and a second zone loyal to the royal government, but with few resources (Boupha 1997). The cooperative-based health system which followed did not last long, but assistance from the International Monetary Fund, the World Bank and the United Nations, as well as development aid funds from Sweden, France, Japan and Australia, helped in the re-construction of the health care system. It was not until the mid-1980s that health reforms became a priority in the political agenda (Boupha *et al.* 2005). The current government health budget serves mainly to support

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salaries and administration costs (Tangcharoensathien *et al.* 2011) and the Total Health Expenditure as a percentage of GDP, remains low (at 1.9% compared to 3.8% in 1995). While out-of-pocket payments, on the other hand, are still high at 39% of Total Health Expenditure (compared to 37.5% in 1995). Despite recent reforms of the health sector, it remains a highly resource-constrained system and is insufficiently developed at all levels (Jönsson *et al.* 2015).

The Ministry of Health (MoH) is responsible for the administration of health care services at the central level, with 18 health divisions at provincial level and health offices at the district level as the main implementers of laws and policies (Kongsap *et al.* 2014). Reports suggest, however, that the public health care system is largely under-utilized (Dodd *et al.* 2009; WHO & MoH Lao PDR 2012). This might be due to poor accessibility to health care services, with the number of hospital beds per 1000 people in Laos reaching just 0.8 (Kongsap *et al.* 2014). The private sector offers a combination of modern and traditional health services and medicines – through hospitals and medical clinics. Laotian traditional medicine, inspired by Indian and Buddhist traditions, still holds an important place in health-seeking practices of the Lao people. Recent reports suggest loose regulation of the private health care sector, which may impede on the quality of healthcare services available to the population (Kongsap *et al.* 2014). Civil society organizations including non-governmental organizations, also play a role in health service delivery, such as the Lao Women Union and Lao Youth Unions (Jönsson *et al.* 2015). Until 1995, health services were free of charge (WHO & MoH Lao PDR 2012), but since 1995, the government established user fees and a referral system. This, however, has not been adequately implemented due to a lack of criteria to identify the poorer members of the population who would be exempt from fees, and a due to a lack of resources to support the system as a whole (Patcharanarumol *et al.* 2009). Four social health protection schemes[37] were introduced in 2001 which were later merged into one National Health Insurance Authority (Ahmed *et al.* 2013; Alkenbrack *et al.* 2013), as Laos strived to achieve Universal Health Coverage by 2020 (Annear & Ahmed 2012). In 2012, however, reports suggest that these four schemes only covered 18.5% of the population (WHO & MoH Lao PDR 2012).

Recent reforms were introduced along with the Seventh Five-year National Health Sector Development Plan (2011-2015) and the Health Sector Reform Strategy (endorsed in December

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[37] Social health protection schemes include: 1. the State Authority for Social Security scheme for civil servants; 2. the Community-based Health Insurance (CBHI) (for monks, members of the religious orders and students); 3. the Health Equity Funds (HEFs) to assist the poor through contributions from the state and international organizations; and, 4. the Social Security Office scheme for enterprise workers, (Annear & Ahmed 2012; National Assembly Lao PDR 2005).

2012). The main focus of health care reforms to date has been on improving access to primary health care services, and improving maternal and child health as well as nutrition as these represent key health priorities for Laos (Kongsap *et al.* 2014; WHO & MoH Lao PDR 2012; World Bank 2016). The main source of funding for the development of the health sector are international donor organisations and donor partners. The literature identifies a few remaining challenges to the health care sector in Laos, the first being the shortage of an adequately trained workforce, with only 2.17 health workers per 1,000 population (WHO & MoH Lao PDR 2012; Dodd *et al.* 2009). Many health care workers were trained in socialist countries prior to the 1990s and this has led to different standards of health care delivery across the country. Low salaries are another reason for this shortage and for the poor productivity among the health care workforce (Dodd *et al.* 2009). Indeed, most health care workers are concentrated in Vientiane where they benefit from better pay. Another challenge is the discrepancy in *access* to quality health services and commodities for communities living in the rural parts of Laos. Some are required to travel up to three hours to the nearest health facility (Thomé & Pholsena 2009). The mountainous landscape and lack of infrastructure in these areas present major obstacles. The communities that suffer most from this lack of access are usually ethnic minorities living in mountainous areas. Laos still suffers from a high burden of infectious diseases including tuberculosis, HIV AIDS and malaria. More recently, Acute Respiratory Infections also represent a high disease burden for the country (Kongsap *et al.* 2014).

7.1.2   Regulating antimalarial medicines in Laos

The main policy for strengthening the health and pharmaceutical sector in Laos is the National Medicine Policy (NMP), first approved in 1993 (NMP 1993) and revised in 2003 (NMP 2003). The Law on Drugs and Medical Products 01/NA (Law on Drugs 2000) and its 2011 Amendment (Amended Law on Drugs 2011) outline the specific rules and regulations pertaining to the management of pharmaceuticals. Appendix 14 (page 364) summarizes information retrieved from a thematic content analysis of these four documents, along with another five policy documents translated into English. The Ministry of Health (MoH) is responsible for the regulation of pharmaceuticals. The Communicable Disease Control Department of the MoH is the principal recipient of Global Fund (GF) grants for the procurement of antimalarials (AMLs). Under the MoH, The Food and Drug Department (FDD) is in charge of monitoring the quality of AMLs and other essential medicines, along with the Bureau of Food and Drug Inspection (BFDI) in charge of inspecting pharmaceutical premises. The FDD is made up of seven divisions, as illustrated in Figure 13 on page 148. The main divisions for the regulation of pharmaceuticals – both modern and traditional medicines

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– are the Drug Control Division, the Traditional Medicine and Supplements Control Division and the Public Pharmacy Control Division.
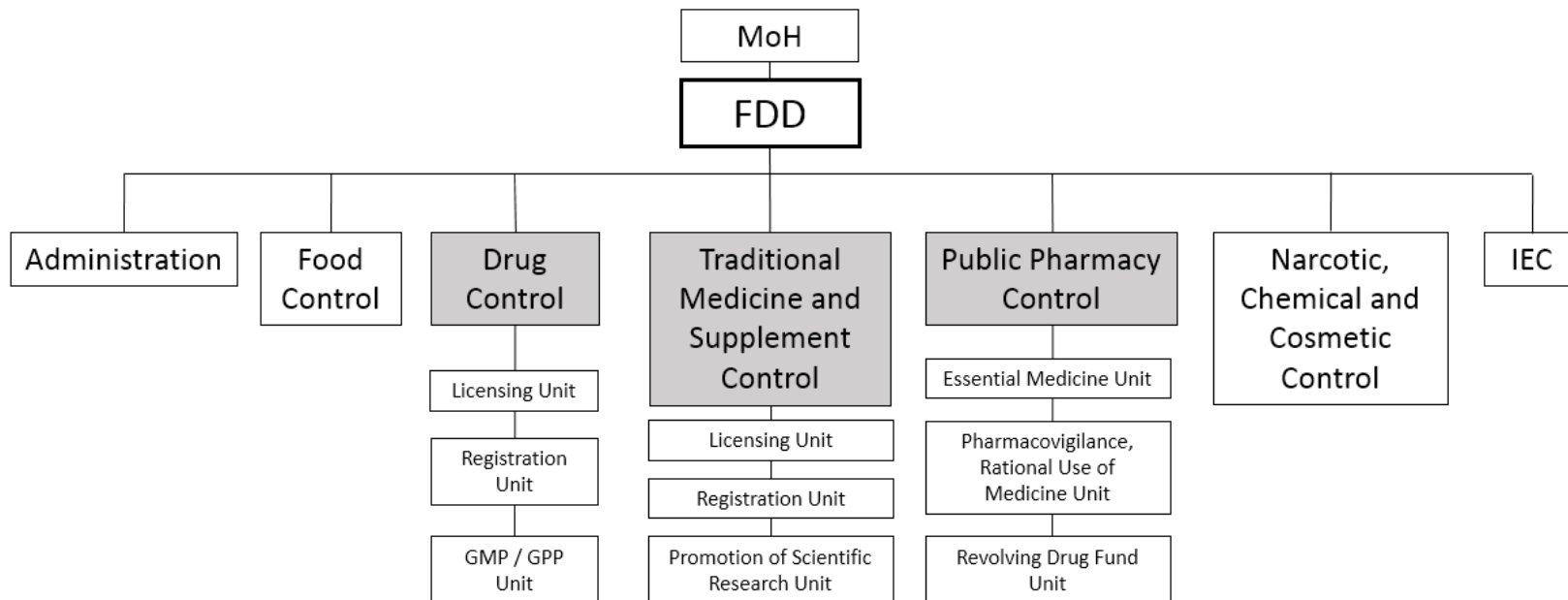
Figure 13 Divisions of the Food and Drug Department of Laos

The FDD's Drug Control Division issues licenses to pharmaceutical outlets, of which there are three categories in Laos known as First, Second and Third Class Pharmacies. First Class Pharmacies can sell a wider range of medicines and are run by a qualified pharmacist, while Third Class Pharmacies may be operated by pharmacist assistants or nurses. These pharmacies are not allowed to sell medicines on the National Essential Medicines List (NEML). According to a researcher from Mahidol Hospital, Third Class Pharmacies no longer exist in Vientiane and such pharmacies are intended to be removed from the system in the near future. Only pharmaceutical outlets that are members of the PPM initiative, malaria clinics or malaria posts are entitled to dispense AMLs. The BFDI replaced the Inspection Department of the MoH in 2014 as the main body responsible for inspecting all licensed premises (drug outlets, manufacturing sites), and to verify compliance with the main rules and regulations across the supply chain of pharmaceuticals. BFDI inspectors are also responsible for inspecting imported pharmaceuticals at formal entry points to verify the products' compliance with quality standards. According to a respondent from the BFDI, there is evidence of law enforcement as demonstrated by the recent closure of eight pharmacies due to their inadequate licensing status. More information on Laos' pharmaceutical regulatory system is available in Appendix 12 on page 356.

The Centre for Malaria Parasitology and Entomology (CMPE) spearheads the malaria program, promotes access to quality ACTs and supports efforts to contain artemisinin-resistance malaria and eliminate malaria all together. With regards to malaria incidence rates, while the general burden of the disease has considerably reduced, achieving the Millennium Development Goal of a 75% reduction (WHO 2016), there have been recent outbreaks in the southern provinces of Laos. Between 2012 and 2013, there were a number of reported malaria cases and deaths (44 deaths in 2012 and 28 in 2013) predominantly among migrant populations working near the southern border (WHO 2014). The main strains of malaria in Laos are *Plasmodium falciparum* (42%), *Plasmodium vivax* (58%) (WHO 2016). Malaria is generally perceived as a disease affecting forest-goers in border areas. 31% of the Lao population still lives in high transmission areas according to the recent Malaria Report (WHO 2016). Recent reports also suggest risks of growing artemisinin resistance endangering those entering Laos via the Thai-Cambodian border in the South (Dondorp *et al.* 2009; Dondorp *et al.* 2011; Ashley *et al.* 2014).

The GF supports the MoH, the Centre for Malaria Parasitology and Entomology (CMPE) and the FDD in its efforts towards case management and to optimize the uninterrupted supply of

malaria commodities, including good-quality and affordable ACTs to vulnerable populations. The GF has been supporting Laos since 2008 from rounds 6 to 8 and disbursed a total of US$ 25 million towards the fight against malaria. The World Bank (WB) and the Asian Development Bank (ADB) are also key donors to support social development programs in Laos. The United States Agency for International Development (USAID) also plays an important role as a funder to support efforts at building capacity for the regulation of AMLs. USAID supports United States Pharmacopeia (USP) as one of the main implementing partners to the FDD and the BFDI in Laos. ACTs were introduced onto the market in 2005 and oAMTs are no longer authorized since 2007 as a first line treatment of malaria. ACTs are available free-of-charge through public health facilities and in private pharmacies, through the Public-Private Mix pilot (PPM) program since 2008. The pilot was expanded in 2014 to include a total of 12 provinces. The chosen first line treatment of uncomplicated malaria is Artemether Lumefantrine and the treatment for severe malaria cases is artesunate injection.

7.2 Policy developments against poor-quality AMLs

From my analysis, I discern three distinct phases in the policy process against poor-quality AMLs in Laos. From 1993 to 2003, the country worked to develop its drug management system, including the rules and regulations for drug registration and licensing procedures. By 2003, evidence of poor-quality AMLs circulating in Laos triggered a period of interest formation around the threat of poor-quality medicines and prompted efforts to strengthen quality monitoring activities between 2003 and 2011, with the support of United States Pharmacopeia (USP) as an implementing partner in this process. From 2011 onwards, the main emphasis appears to be on fostering more cross-border cooperation and increasing transparency to support the implementation of planned efforts against poor-quality medicines. The policy process is illustrated in the timeline (see Figure 14 on page 151), which provides a chronological overview of the laws and policies introduced over time to regulate pharmaceuticals and their quality in Laos. For an overview of the policy actors involved in the regulation of medicines in Laos, see Appendix 13 (page 360).
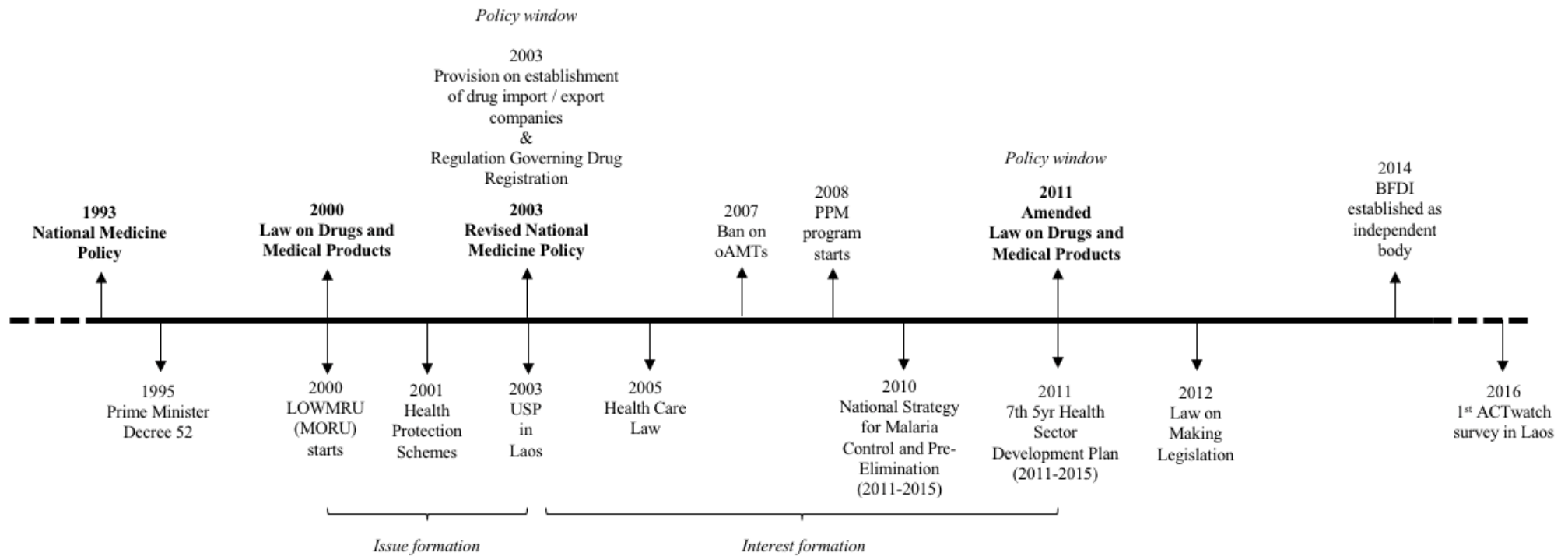
Figure 14 Timeline of policy developments for pharmaceutical regulation in Laos

7.2.1 Phase I: Building a drug management system (1993-2003)

7.2.1.1 SIDA and health sector reforms

Driven by socioeconomic developments in the country since the 1990s, Laos undertook a process of reforming its health sector (Kongsap *et al.* 2014) with the support of international development partners. Simultaneously, there were continuous efforts to strengthen the drug regulatory system to improve access to quality medicines between 1993 to 2003. This included the development of rules and regulations for the registration of pharmaceuticals and the licensing of pharmaceutical manufacturers, importers and distributors. Before the National Medicines Policy was in place, the delivery of drugs to pharmacies was a challenge and there were reports of mismanagement of donated pharmaceutical stocks that expired before reaching patients, or that failed to reach the right patients altogether (Jönsson *et al.* 2015; Thomé & Pholsena 2009). Loosely regulated private pharmacy outlets proliferated following the switch to an open market economy in the late 1980s, which led to the smuggling of many pharmaceutical products (STK25). These challenges drove support for drafting a National Medicine Policy (NMP 1993). This was drafted and approved in 1993, with the help of the Swedish International Development Cooperation Agency (SIDA) as the main implementing partner in this first phase of the policy process. The NMP was aimed at guiding the general development of a young health and pharmaceutical sector.

7.2.1.2 LOWMRU and the role of evidence

As a key focusing event of this phase, the Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit (LOWMRU) was established in 2000. Professor Paul Newton at LOWMRU first officially reported the presence of poor-quality AMLs in Laos, and the public health danger this represents in 2001, in a study on the quality of artesunate samples from shops, pharmacies and hospitals in five countries across Southeast Asia (Newton *et al.* 2001). While a relatively small sample of eight tablets was collected in Laos, 38% of those were deemed 'fake'. This was the first reported evidence of poor-quality antimalarial medicines (AMLs) in Laos available in academic literature. LOWMRU continues to gather evidence on medicine quality in Laos, evidence that serves as guidance for policy makers and legislators. Subsequent publications by the research unit alerted to the urgency of cross-border action to prevent the spread of artemisinin resistance, potentially exacerbated by the availability of poor-quality AMLs. The work of LOWMRU also served to uncover the source and smuggling routes of at least some poor-quality AMLs and raise attention among donor organizations, attracting funding and support from the development sector.

In Laos, LOWMRU benefits from a close working relationship with several state-level actors including the FDD. As a research unit, LOWMRU brings together a network of actors through knowledge sharing. In its capacity to raise awareness about this challenge and gather political support for action to improve access to quality medicines, LOWMRU acts as a policy entrepreneur. The work of LOWMRU triggered a phase of issue and interest formation in Laos by 2003. With regards to sharing knowledge and expertise to strengthen drug regulation, however, Jönsson *et al.* (2015) note that since the mid-1990s, Thailand and Laos set up a bilateral health sector cooperation committee to learn from Thai expertise in strengthening health systems. From early on, Laos has been open to using scientific evidence to guide policy reforms and to sharing technical knowledge with neighbouring countries in support of efforts to strengthen the health sector. While it is uncertain to what extent scientific evidence influenced policy developments, there may be a link between the evidence produced by LOWMRU and the increasing attention from the Lao government towards the policy problem of poor-quality medicines.

7.2.1.3   Poor-quality medicines defined as counterfeit or unregistered

The Law on Drugs and Medical Products was introduced in 2000 and outlined more specifically the principles of drug management. Additionally, the (2003) Regulation Governing Drug Registration no. 1441/MoH (2003) provides more detail on registration procedures for pharmaceutical products in Laos. Regardless, poor-quality medicines were still defined predominantly as 'counterfeit' or 'unregistered' medicines. At the outset, the definition of what constitutes a poor-quality pharmaceutical product in Lao laws and regulations, remains unclear due to the inconsistent use of a variety of keywords related to medicine quality since 1993. The main term used in the definition of poor-quality medicines in the NMP was 'counterfeit' – a choice of terms that inadvertently emphasized the trade infringement aspect of the problem over its health implications. This may have been a deliberate choice, although the data collected does not suggest a strong inclination towards the protection of intellectual property rights for pharmaceutical products. More likely, the choice of term echoes the preferred terminology used in global communications around the problem of poor-quality medicines in the early 2000s.

The definition of poor-quality medicines available in the Law on Drugs and the Regulation no. 1441, still refers to a 'counterfeit drug' as an '*imitation* of a drug product, which is produced, distributed and legally registered'. Regulation no. 1441 (section 6, article 17) also states that 'it is prohibited for individual and juristic persons to counterfeit the registered drug

formulas, trade names or generic name'. This clause exclusively refers to drug counterfeiting and trademark infringement. These last two definitions not only focus on drug counterfeit but speak of imitations of *registered* drugs only, thereby omitting from the scope of these laws any *falsified* medicine circulating in the country whose original brand is not registered in Laos. Penalties were established against individuals who produce or sell counterfeit or unregistered medicines. Regulation no. 1441 (2003), for example, establishes incremental levels of penalties for violations of regulations concerning pharmaceutical management. Any individual who sells 'counterfeit' or 'unregistered' medicines will see all drugs confiscated after a first violation, receive an additional fine as well as confiscation on second offence, and will be fined at 200% of the total value of all drugs in stock on third offence, with permanent closure of premises. Additionally, the Provision on the Establishment of Drug and Medical Equipment Import-export Companies (1442/MoH 2003) establishes measures against importers of such medicines.

7.2.2   Phase II: Interest formation and quality monitoring (2003-2011)

7.2.2.1   Quality assurance

Results from a study published by Dondorp and colleagues (Dondorp *et al.* 2004) found that samples of artesunate tablets in Laos were 'counterfeit' after both chemical testing and package verification. Additionally, this study highlights the use of sophisticated technology to replicate the genuine 'Guilin Pharma' hologram on the packaging from falsified artesunate tablets in southern Laos (Dondorp *et al.* 2004). Another investigation of fake artesunate samples, collected 115 further samples in Laos with a total of 49.9% fake artesunate with either no or insufficient quantities of the Active Pharmaceutical Ingredient (API) (P. Newton et al. 2008). While in a further study, 180 outlets in 12/18 province were surveyed in 2003 to record the presence of oral artesunate monotherapies (oAMTs) (Sengaloundeth *et al.* 2009). Out of 180 outlets, 25 sold banned oAMTs, and 22 of those were deemed 'counterfeit'. Although these findings provide vague estimates of the scale of the problem, such evidence may have prompted the FDD and implementing partners to improve efforts against poor-quality medicines in Laos.

The revision of the National Medicines Policy in 2003 formed a window of opportunity to strengthen quality monitoring operations. The revised NMP (2003, Article 2.3) emphasizes first and foremost monitoring on drug *safety* and *efficacy* for consumer protection rather than addressing the *crime* of falsified medicines. The focus of this policy is primarily on quality assurance, stating that 'Quality assurance is a wide-ranging concept covering all matters that

directly or indirectly influence the quality of a product' (Article 4). The revised policy states that pharmaceutical products proven unsafe or ineffective will be recalled and that Marketing Authorizations may be withdrawn, if a product are subsequently deemed non-compliant with submitted quality standards or found to be unsafe for consumers. While the Law on Drugs (2000) already called for the establishment of Toxicology Information Centre, the revised NMP strengthens pharmacovigilance procedures. Article 4.5, for example, states that the MoH should use existing international networks for quality assurance such as the Electronic System or Drug Information Exchange in the Western Pacific Region, to share information on drug regulatory decisions in other countries and improve Laos' efforts in the quality assurance of new drugs. Article 2.10 of the revised NMP also encouraged the government to 'identify and to promote research activities, which will provide evidence based decisions for interventions for strengthening the implementation of the NMP'. This is testimony once again to a strong focus on evidence-based policy making, with an openness to research and external collaborations. This emphasis is potentially a legacy of the involvement of SIDA and the Karolinska Institute of Stockholm as international collaborators in the drafting of the NMPs (Jönsson *et al.* 2015).

7.2.2.2 USP and drug quality monitoring activities

To support the implementation of drug quality monitoring activities, USP has provided invaluable technical assistance to the FDD and the BFDI, since it started its operations in Laos in 2003. The USP Promoting the Quality of Medicines (PQM) program proved crucial in strengthening drug quality monitoring operations in Laos. In its role as a main technical partner to the FDD and the BFDI, USP acts as policy entrepreneur along with LOWMRU for efforts against poor-quality AMLs, raising awareness about the risks of poor-quality medicines in the supply chain and harnessing political will to improve quality control of medicines. More specifically, USP supports post-marketing surveillance efforts and the quality inspection of AMLs, for example through the development of laboratory standard operating procedures, as well as a clear testing and sampling methodology. A yearly average of 250 samples in each province are tested on site using the USP-sponsored minilab. All suspect samples are then forwarded to the national laboratory, known as the Food and Drug Quality Control Centre (FDQCC). If no samples are suspect, 10% of the initial sample is forwarded through regardless. USP supports capacity development for the national lab in preparation for a potential international ISO certification for its testing methodology in the future. It also supports laboratory staff in their learning of English to facilitate this process. The PQM program, as an initiative, is present in more than one country throughout the GMS, and not

only supports the capacity of the Lao government to improve their quality monitoring activities, but creates a region-wide network among Mekong countries to share information and expertise on efforts against poor-quality medicines.

As part of the government's efforts to improve access to quality AMLs, the sale and distribution of oAMTs was banned in 2007. Since 2008, the Public-Private Mix (PPM) program led by the FDD, with technical support from the WHO and funding from the GF, has been a key initiative to improve access to good quality medicines and to exercise some control over the private sector distribution of essential medicines, as suggested by respondents from the CMPE. The first initiative within this PPM program was to map private health facilities and pharmacy outlets in Laos to subsequently invite them to a training course on the use of RDTs for malaria diagnosis and on effective reporting of malaria cases. After this course, private sector outlets were given the option to opt into the PPM scheme with the signature of a yearly contract. Those that agreed to the terms (approximately 250 pharmacies to date) were given permission to distribute first line treatments to confirmed malaria patients. Despite these initiatives, respondents suggested that oAMTs are reportedly still available through unofficial channels (Skerrit *et al.* 2014).

7.2.2.3   Improving equitable access to quality medicines

Most policy and legal documents in this second phase of the policy process emphasize improving *access* to medicines, focusing not just on safety and efficacy and consumer protection, but on key issues of equitable access to health services and access to medicines for vulnerable populations. This emphasis is important because it translates into a priority focus on strengthening health systems in support of the principle of universal health coverage. The first NMP (1993) already emphasized the goal of 'ensuring *availability* and rational use of high quality medicines at low cost, with a focus on *vulnerable populations in remote areas*'. Additionally, the overall objective of the revised NMP (2003, Chapter 1) includes ensuring '*equitable* availability and affordability of essential medicines'. Under Article 8.6, the NMP 2003 focuses on 'economic strategies for medicines' to finance access to essential drugs and encourage cost recovery by harnessing donor financing to provide essential medicines for all, including for remote and vulnerable populations. Furthermore, the Law on Health Care (2005), which details the health insurance system, reiterates the need to: 'improve the quality of health care to ensure that the whole population and in particular women and children, poor citizens and those who live in remote or isolated areas, have a good state of health' (Article 5).

Despite an interest in the problem of poor-quality medicines, definitions of poor-quality medicines in rules and regulations drafted between 2003 and 2011 remain vague. The 2003 regulation on import-export companies, for example (Article 14.4), states that the 'import-export of *unqualified* drugs, *counterfeit* drugs, *drugs from improper sources*, incorrect packaging….and all types of *banned* drug are *prohibited*'; hereby using in its definition of poor-quality medicines a wide array of terms from 'unqualified' to 'banned' vs. 'prohibited', none of which are defined further in the document. The term 'falsified' still does not appear in this definition.

7.2.3   Phase III: cooperation against substandard medicines (2011-2016)

7.2.3.1   Cross-sectoral cooperation

The third phase, from 2011 onwards, is characterised by a general intention to enhance cross-border cooperation to improve efforts against poor-quality. The revised NMP already paved the way towards more cooperation for quality monitoring activities, by encouraging the MoH to act against poor-quality medicines in cooperation with police, customs and other relevant agency bodies. Following additional evidence of poor-quality AMLs circulating in Laos (including results from the study by Sengaloundeth 2009[38]), there was an attempt to clarify the roles and responsibilities of relevant bodies within the drug regulatory framework, and to improve checks and balances and systems in place to enforce existing policies. The Amended Law on Drugs and Medical Products in 2011 was a second policy window of opportunity to do so, while strengthening post-marketing surveillance. In Article 37, the Amended Law on Drugs (2011, Article 37) specifies the obligations of suppliers to report any '*harmful effects to the health of users* resulting from the use of poor-quality, unsafe drugs and medical products'. Article 36 encourages users themselves to report 'substandard or unsafe' medicines, thereby placing the medical responsibility on the user. In Article 42, the Law reiterates the responsibility of the MoH to handle propositions related to drug quality standards and to support the enforcement of the regulatory framework, from the registration of medicines, the licensing of pharmaceutical business operators to quality control standards. Subsequently, efforts to divide responsibilities on quality inspections led to the establishment of the BFDI as an independent inspection agency in 2014, marking an important structural change in quality monitoring of pharmaceuticals. We have yet to see the benefits of this change, and will have to wait for a future appraisal. Due to the vague terminology around poor-quality medicines in

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[38] Samples of oAMTs in this study were collected before the 2007 ban on oAMTs in Laos and may results published in 2009 may not be an accurate reflection of the situation in this third phase.

the Amended Law[39], this law still falls short of attributing responsibility or accountability for the pharmaceutical crime of medicine *falsification.*

7.2.3.2 Defining substandard medicines

The Amended Law on Drugs (2011, Article 39.3) explicitly prohibits any pharmaceutical business operators from selling drugs that are 'counterfeit, substandard, deteriorated or expired', and details further penalties for the infringement of its clauses. While these penalties serve to strengthen the system against drugs of poor-quality medicines, the extent to which they are enforced is unknown. The Amended Law is first time that the term 'substandard medicine' is used instead of 'non-standard drug' (2011, Article 3.4.), where a substandard medicine is defined as 'a modern drug or traditional medicine, the composition of which is not consistent with its registered formulae'. This reflects rising concern around the problem of substandard medicines, and the implications of these for rising antimicrobial resistance. A repeat study of antimalarial drug quality conducted in 2012 suggests that the presence of falsified AMLs in Laos has considerably reduced since 2003, with substandard AMLs remaining of concern (Tabernero, Newton, et al. 2014). This was the first study to measure the change in prevalence of poor-quality medicines over time, including AMLs and other medicines. From a sample of 1,200 tablets of 158 different AMLs collecting from 147 outlets in five southern provinces with a high malaria incidence, 6.3% of the outlets were found to sell oAMTs. All samples contained the correct API and had no evidence of falsification, however 9 samples were found to have a lower dosage of the API. Authors add that evidence of falsification is hard to discern and, for samples with lower dosages of API, it is difficult to tell whether those may be classified as substandard or degraded. This study, however, suggests that the situation in Laos had improved by 2012 in terms of access to good quality AMLs, with substandard AMLs being more of a problem than falsified AMLs. Such evidence, along with rising awareness about the threat of artemisinin resistance also present in the Southern

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[39] Previous definitions of poor-quality medicines are superseded by the definition available in the Amended Law on Drugs (2011). In Article 3.3, the revised law defines 'counterfeit drugs' as 'any modern drugs, traditional medicines, medicinal natural resources, cosmetics, health supplement, medical devices, controlled chemicals and dangerous chemicals which are intentionally falsified or imitated or copied from the products which are produced, distributed and legally registered, for the trade benefit purpose'. This definition contains the term 'imitated', which refers to copies of a product and therefore alludes to Intellectual Property (IP) Infringement. Interestingly, however, this definition also refers to 'intentionally falsified' medicines and therefore refers to the notion of intent which is at the core of the definition of this pharmaceutical crime. In this clause, the definitions of 'counterfeit' and 'falsified' medicines are merged into one. Despite a more encompassing use of terminology, the reference term remains 'counterfeit medicines' and leaves room for confusion.

Provinces of Laos, seems commensurate with the emphasis on promoting the rational use of medicines and strengthening efforts against substandard medicines including oAMTs.

7.2.3.3   Regional challenge of substandard medicines

Policy actors gradually realized, from the evidence submitted at the regional level, that the problem of poor-quality AMLs was a regional health challenge, requiring policy coordination across borders. The revised NMP already promotes 'international technical cooperation' through ASEAN working groups on technical cooperation in pharmaceutical or the ASEAN consultative Committee for Standards and Quality, with the objective of harmonizing policies across the region (Article 13). In the pursuit of improving stakeholder collaboration to strengthen the regulatory framework, the revised NMP (2003) also emphasizes the need for more data to inform the development of Laos' health system. Despite these clauses encouraging cross-sectoral collaboration, however, results suggest a lack of a strong policy subsystem to facilitate cross-sectoral cooperation against poor-quality medicines. The Amended Law on drugs (2011, Article 7) further encourages international cooperation with foreign countries or regional organizations through the exchange of information, science, technology and through capacity building programs. Additionally, the revised Customs Law (2011, Article 75) encourages cooperation between the MoH and other government offices at border check points. This same law also refers to Agreements of Greater Mekong Sub-region countries to regulate the movement of boats on the Mekong to prevent smuggling of illegal goods by river transport (Article 71).

Despite these various clauses promoting cross-sectoral and international cooperation, it is unknown how regularly suggested meetings and exchanges of information take place, and how these might have negatively or positively impacted on the regulatory capacity of the MoH on the quality of pharmaceuticals. This favourable approach towards more cross-border cooperation to learn from neighbouring countries, echoes government-level respondents' concerns regarding the lack of funding and capacity or capability nationally to enforce existing laws. This also relates to an admitted reliance on development initiatives to improve access to health services and to strengthen the health regulatory system. In this respect, government-level respondents often expressed the need for more scientific evidence to justify the allocation of further funding in support of government efforts to fight against poor-quality medicines.

7.3 Perceptions of the problem of poor-quality medicines

In this section, I present the findings from 17 stakeholder interviews conducted in 2015 in Vientiane with representatives from the government (9), members of implementing partner organizations, donor organizations, as well as the owner of a domestic pharmaceutical manufacturing site. The main themes that emerged from the data under the six master frames are summarized in Table 14 on page 161. The process of data collection in Laos was facilitated by the Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit (LOMWRU). LOMWRU, headquartered at Mahosot Hospital in Vientiane, benefits from a close working relationship with the Ministry of Health (MoH) and the Food and Drug Department (FDD). With the help of Professor Paul Newton from LOMWRU, an advisor on this project, I was able to rapidly identify government-level respondents, all of whom were very willing to discuss this sensitive topic. I welcomed the openness with which most respondents shared information on the situation in Laos, some of whom did not shy away from being critical of the regulatory system or acknowledging the weaknesses in terms of capacity to implement existing laws. Most interviews, however, were not recorded. The interviewing process was conducted in English although some respondents were more at ease with French. It was an advantage to be able to switch from one language to the other during our discussions. With regards to accessing information on official laws and policies in Lao PDR, both the FDD website as well as the online Lao Trade Portal, provide access to English translations of most Lao Laws and Policies pertaining to the health sector. The article by Jönsson *et al.* (2015) provides useful supplementary information regarding the gaps and challenges of the pharmaceutical regulatory system in Laos.

Frame	Observations
Regulatory	Both categories of respondents pointed to the low capability and limited financial and human capacity within the NRA to regulate pharmaceuticals effectively. Government level respondents add that cross-sectoral cooperation is an added challenge to the implementation of rules and regulations.
Political	Non-government respondents suggest that there is still a lack of political commitment resulting from weak accountability mechanisms, the untransparent management of supply chains and the uneven enforcement of rules and regulators, particular in provincial and district areas. Government respondents explain that low political will is due to the lack of data on the problem of poor-quality medicines.
Economic	Some respondents referred to the economic status of Lao PDR , the challenge of foreign investment exacerbating income disparity, and the low public health sector budget as a challenge to guaranteeing access to quality medicines.
Security	Both categories of respondents refer to Laos' position as a transit country, prone to illegal smuggling, as a challenge for the circulation of poor-quality medicines. Government respondents clearly portray Laos as a 'victim' among its GMS neighbours.
Medical	Most references to this frame were indirectly made through the security or the health systems frame. Only a few respondents explicitly mentioned the irrational use of medicines as a factor contributing to the problem of poor-quality medicines and some referred to the challenge of drug resistant malaria as a concern.
Health Systems	Both categories of respondents suggest that stock-outs of medicines due to inefficient reporting and quantification processes, as well as poor health infrastructure, impact access to quality assured medicines, especially for MMPs. Non-government respondents add that the high number of unlicensed drug outlets or pharmacy outlets run by unqualified personnel with poor distribution practices, also contributes to the circulation of poor-quality medicines.

Table 14 Summary of frames detailing stakeholder perception of factors contributing to the circulation of poor-quality medicines in Laos

7.3.1 Regulatory Frame

7.3.1.1 Inadequate regulatory framework

Both government and non-government respondents discussed the poorly adapted nature of the Lao regulatory framework for preventing the circulation of poor-quality medicines. Some mentioned discrepancies regarding drug registration requirements, stating that some products do not require registration in Lao PDR. These include donated drugs, which are also exempt from customs duties, as stipulated in the Revised Customs Law (2011, Article 56). GF-funded AMLs may bypass registration procedures if they are procured through WHO pre-qualified manufacturers. Although the drugs must still comply with the quality standards set by the (2011) Law on Drugs, these exemptions might make it more challenging to depict poor-quality stocks – especially of a falsified nature – at ports of entry. Both government and non-government respondents referred to discrepancies regarding licensing requirements for domestic drug manufacturers in Laos. In principle, all licensed domestic manufacturers should be GMP certified, but in practice this is not a requirement for licensing. While there is a national GMP certification program in place, managed by the FDD, respondents pointed out that no domestic manufacturing site has achieved international GMP certification to date. The lack of enforcement of GMP requirements, respondents noted, might be problematic for the circulation of potentially substandard medicines other than AMLs (which are no longer produced or procured locally).

Government respondents added that the regulation of medicines along the supply chain was sub-optimal, leading to the proliferation of substandard medicines:

> Sometimes, it's from the transportation…the storage condition(s) in the rural area(s) [are] very poor. (STK21G_NRA20150408)

Additionally, it was mentioned numerous times that the lack of regulation of private sector outlets remains a danger for the continued circulation of poor-quality medicines:

> Poor-quality medicines cannot be stopped from reaching the private sector. (STK24G_NRA20150508)

With regards to post-marketing surveillance activities, respondents also reported that the BFDI is largely under-resourced, both financial and in terms of human capacity, to carry out its mandate effectively. Despite incentives to enforce existing regulations, respondents noted that inspections are not regular, primarily due to a lack of human and financial capacity within the

BFDI and the FDD. Another respondent pointed out that the most common type of inspections is 'by advance notice' instead of routine or emergency (unannounced) inspections (STK24G_NRA20150508). This, the same respondent added, reduces the opportunity for inspectors to notice abnormal practices within pharmaceutical outlets or manufacturing sites. Such factors, respondents agreed, make it more difficult to pick up poor-quality medicines on the market.

7.3.1.2   Enforcement capacity

Both categories of respondents also alluded to the lack of enforcement capacity to successfully implement what was perceived as a comprehensive regulatory framework, on paper at least. Government respondents openly acknowledged the lack of human resources and financial capacity of the MoH, the FDD and the BFDI. When discussing evidence of inspections and enforcement with respondents, only one example came to light; the closure of a pharmacy in Attapeu province in 2010. The literature also refers to the weak planning and overseeing capacity and capability of government officials in implementing drug regulation (Ahmed *et al.* 2013). A government representative admitted for example that penalties for unregistered medicines were not implemented effectively (STK24G_NRA20150508). Another added that:

> Laos has a lot of regulation, documentation, laws on the books, but enforcement is almost non-existent. (STK26NG_INGO20150409)

This 'lack of rigor' as the respondent added (STK26NG_INGO20150409), creates an environment where poor-quality medicines are free to circulate. Respondents from the BFDI itself expressed despair at the challenge of regulating a complex supply chain of pharmaceuticals, with the currently limited human and financial capacity and technical capability of the Lao regulatory and inspection agencies. They also explained that regulatory agencies do not always have the authority to enforce the regulations accordingly. A respondent from BFDI for example, referred to this issue of mandates:

> It is very difficult to perform the enforcement… because our inspectors do not have enough power to inspect… (STK23G_NRA20150508)

In terms of technical capacity, both government and non-government respondents added that while the FDQCC is currently working to improve its standard operating procedures, the laboratory capacity to test medicines samples within Laos remains limited, therefore narrowing the scope of post-marketing surveillance activities.

> [I]f we were to just test the average drugs in the average pharmacy on a regular basis, we would find a lot more substandard medicines than we do find but we have these only rare once every couple of years funding to do testing and it's not enough testing, it's not a big enough sample and so we don't really know how poor the quality is in the average pharmacy - but I believe that it's quite poor. (STK26NG_INGO20150409)

The FQCC is largely under-resourced and lacks the required SOPs. While it is currently certified for testing one pharmaceutical product only (an antibiotic), laboratory staff are currently working to improve its capacity with technical support from USP aiming achieve ISO 17025:2005 certification and subsequently WHO pre-qualification status. Respondents from the FDD explained, however, that the current lack of adequately trained staff is a challenge, partly caused by a high turnover of trained staff leaving the regulatory agency for better paid jobs with partner organizations.

The BFDI added that the lack of financial resources to conduct joint investigations and to arrest violators of the law is also a challenge:

> We try to create activities together with the stakeholders, but we have limited financial support. Also, we have a plan, joined together to investigate but it's just a plan. The budget is not coming. (STK21G_NRA20150408)

This point seemed to bear some weight in our discussions, as more than once government-level interviewees sought my advice for potential funding opportunities to support their activities.

Respondents also explained that enforcement efforts are uneven across the country; often more sustained at the central level, and more diffuse in provinces further away from Vientiane:

> We need to improve the capacity of the local staff to strengthen their competency in terms of regulation and control [of] such kinds of medicine. Until now we cannot delegate to the district to do on their own because of insufficient staff especially pharmacists in the district level - we just delegate to the provincial health office to help, therefore we cannot oversee everything in the country in terms of medicine control. (STK30G_MoH20150410)

Enforcement efforts at the border areas are perceived as particularly patchy. During my visit, I travelled to the Thai-Lao Friendship Bridge, located 20 kilometres away from Vientiane, southwards along the Mekong River at the border with Thailand. The customs representative I interviewed at this spot, admitted that stocks from trucks coming into Laos and driving onwards to provincial destinations were not systematically controlled – this was also due to

the sheer number of vehicles and people crossing this bridge daily. In a further illustration of lack of enforcement of existing rules and regulations, another government respondent confirmed that there have been no arrests or confiscations of stocks so far in line with medicine quality issues (STK23G_NRA20150508).

Considering these limitations, respondents argued for the need to prioritise regulatory efforts. One respondent explained that enforcement priorities for Laos over the last decade have been targeting opium production and trade – a huge public health concern in the country as well deviating funds for the management of the quality of AMLs. Other respondents argued for the need to focus on the implementation of the ban on oAMTs and to optimize the legal supply chain of pharmaceuticals before addressing the challenge of poor-quality essential medicines:

> How customs can do a good job in the checkpoint to really implement the regulation of banning monotherapies to this area. I am not talking about the substandard or counterfeit yet…we are now fighting oral monotherapy – which is banned, but can still be found. (STK31NG_IGO20150410)

7.3.1.3   Stakeholder cooperation

Having acknowledged the challenges to regulatory enforcement, government officials regularly referred to the necessity for more cross-sectoral and cross-border cooperation to support access to quality medicines. Firstly, BFDI staff explained that current collaborations between BFDI inspection agents, police and customs are ad-hoc and unsystematic. Respondents expressed hope for this the institutionalization of cooperation efforts:

> But for the time being there is not structured mechanisms. Its meetings, discussion and maybe in the future a structured mechanism? (STK23G_NRA20150508)

BFDI inspectors are only mandated to inspect *licensed* pharmacies. However, poor-quality medicines are perceived by all respondents as a problem that goes beyond the licensed outlets, and efforts to uncover the circulation of poor-quality AMLs therefore means working together with police and customs officials. Seeing as customs officials are not trained to recognize poor-quality or unregistered medicines, the BFDI has an important role to play at border checkpoints. A law enforcement official further explained:

> Whether the products transported are counterfeit or not is difficult for a customs official to tell as it is not their specialism. (STK27G_LEA20150409)

Government respondents commented that unsystematic cooperation between health inspectors, police and customs fails to support enforcement efforts. They added that instances of cooperation are even more infrequent at the peripheral level:

> There needs to be cooperation with police and customs. At present cooperation is rare and only at the central level and not very regular at all. There is little cooperation at provincial or checkpoint level. (STK29G_NRA20150410)

Government respondents also mentioned that Lao customs officials cannot control the borders on their own, but require support from the neighbouring countries at international checkpoints to address the smuggling of poor-quality medicines between Mekong countries. Cross-border cooperation at customs level could be useful, they argued, to obtain information on the routes of the poor-quality medicines. Such cooperation could therefore support crucial evidence gathering to steer future regulatory efforts at the regional level. Many highlighted numerous challenges to cross-border cooperation. Some explained the sensitivity around the problem of poor-quality medicines, which impedes on cross-border cooperation efforts with countries such as China, when it comes to uncovering trade routes. Having acknowledged limitations in enforcement capacity, government respondents also concurred that support from implementing partner organizations (USP for technical support in post-marketing surveillance for example) or regional bodies is crucial. USP facilitates cross-border cooperation on sample testing by encouraging cooperation for joint investigations with university laboratories at Chulalongkorn University. While there is evidence that government officials are aiming towards more cross-border cooperation, the outcomes of current policy coordination efforts through ASEAN are still perceived to have relatively insignificant impact or benefit for Laos, as stated in the following quote by a government respondent:

> We try to make a cooperation [through] the ASEAN [for] so many years ago…They organize meetings, they train us about the methodology and how to deal with the AMLs also, but the benefit from these activities we perform is not much. (STK23G_NRA20150508)

Regardless, government respondents acknowledged the value of sharing the burden of registration procedures for new medicines with neighbouring countries through an ASEAN harmonized registration process. Such a system, respondents argued, could provide support to bear some of the burden for smaller economies like Laos. Such statements offer testimony to the perceived value of regional cooperation to improve access to quality medicines.

7.3.2 Political Frame

7.3.2.1 Political will and accountability

The political frame was dominant mainly amongst non-government respondents. Besides acknowledging weak capacity and capability to enforce existing regulations, respondents highlighted a lack of concrete political commitment to enforce policies and laws to monitor the quality of medicines. The literature suggests that the enforcement of existing laws and policies has not been without difficulties (Jönsson *et al.* 2015). The sustained support from SIDA and Swedish partners in monitoring the implementation phase of the NMP did help enforce some of the guidelines listed in this policy, while the implementation process for the Health Care Law for example has proven more challenging (Jönsson *et al.* 2015). Other suggested challenges that may have delayed the implementation process include weak financing and leadership, as well as the difficulty of accommodating the needs of minorities and managing the relationships between all the different health financing schemes (Annear & Ahmed 2012). Most government-level respondents did, however, demonstrate a strong awareness of the challenge of poor-quality medicines and the associated public health risks.

> Fake medicines are a big problem, mostly for essential medicines including antimalarials and antibiotics. (STK20G_NRA20150407)

During the interviewing process, many respondents provided detailed information about the current laws, and the incremental penalty system, as evidence of a strong awareness of regulatory frameworks in place. A respondent from the BFDI carefully highlighted the difference between 'fake' and 'substandard' medicines, a distinction that was not always enforced in discussions. While this might be testimony to strong political interest towards the policy goal of access to medicines, discourse from non-government respondents suggest otherwise. One respondent emphasised that the weak enforcement of the regulatory framework is due to a lack of sustained political commitment, rather than a generalized financial constraint:

> It's not something about the level of the economy…If people commit to fight against the fake medicines I think it's possible… it is the willingness or the commitment of the government to cope with the problem. (STK36NG_Academia20150413)

This same respondent commented that further advocacy at higher levels of the government is required to keep the momentum of efforts against poor-quality medicines. A respondent from

an implementing partner organization added that political culture and a lack of political will in Laos can stand in the way of implementing efforts for the effective regulation of pharmaceuticals:

> …Enforcement is almost non-existent. Some of that comes down to budget, and some of that comes down to just culture – nothing is really enforced if you don't want it to be enforced. (STK26NG_INGO20150409)

Accounts from other government-level respondents pointed to a lack of willingness to shoulder accountability for the potential circulation of poor-quality medicine in private sector outlets, deemed to be beyond the responsibility of the FDD. As seen previously, a respondent from the FDD explained that while there is no hard evidence of falsified medicines circulating in Laos since 2005, the FDD cannot stop those from reaching the private sector outlets, thereby dismissing it as a problem under the FDD's responsibility. A respondent from the BFDI also mentioned that regulators between the central and provincial levels of government shift the blame for the circulation of poor-quality medicines to one another:

> It is related to trust among the persons who perform the enforcement together – they may think that those products come from the capital for example – because the capital [has] lots of companies, why don't you manage or control them. Some people may say that these products come from the province who have the borders with other countries - they make that discussion [debate], never finish. (STK23G_NRA20150508)

Government respondents also referred to the political sensitivity around this topic with regards to the reputation of the country, which may explain this lack of willingness to delve into this problem further:

> It affects politics by making other countries think that for example, if we find counterfeits in the country, other countries may think that we have low regulation or that law in those countries may be poor – or that there may be corruption or something, for the staff official to perform the enforcement. (STK21G_NRA20150408)

Another non-government respondent added that reliance on external funding and support to enforce existing regulations, is dangerous as it leads to complacency within the government, where officials rely too much on the work of implementing partner organizations to answer their mandates. This may be commensurate with a reported lack of political will.

7.3.2.2 Transparency and corruption

Various respondents concurred that the lack of commitment to tackle the problem of poor-quality medicines is mainly due to a lack of evidence or information about the scale and nature of this challenge. Government respondents argued that this results in low priority granted to the efforts against poor-quality medicines and mediocre budget allocations for drug quality monitoring. Government level respondents further argued that this lack of data transparency, hinders their ability to seek further funding to support post-marketing surveillance activities and to guide the regulators on where to invest their meagre resources. A respondent from the FDD noted that the current infrastructure does not allow for the systematic collection of samples, but that in return, the lack of evidence to show to regulatory authorities doesn't help justify investments to strengthen the laboratory facilities.

Under this same theme, non-government respondents pointed to a different issue. One respondent from an implementing partner organization mentioned that the information that is available is not always considered, arguing that decisions are driven by political preferences rather than evidence:

> Decision-making is by decree - it's a political process it's not necessarily based
> on information but rather what is politically wanted.
> (STK26NG_INGO20150409)

Another respondent from an international organization explained that this lack of transparency is also apparent in the management of the available funds, that the 'lack of traceability of funds' is a problem and that the government 'need[s] to solve the transparency issue' (STK38NG_Academia20150413). Non-government respondents explained that the politically sensitive nature of this challenge leads to un-transparent management of funds, and impedes efforts to cooperate across borders. This lack of transparency, it is argued, translates into a lack of information sharing with the public. One non-government respondent explained that despite awareness of the dangers of poor-quality AMLs, only one poster was made since 2001 (STK32NG_IGO20150410).

Some respondents also referred to instances of corruption within government, which could explain the lack of enforcement of existing regulations to improve access to medicines.

> Enforcement is almost non-existent. Some of that comes down to budget, some
> of that comes down to [political] culture – nothing is really enforced if you don't
> want it to be enforced. (STK26NG_INGO20150409)

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The same respondent explained that vested interests and corruption (often driven by low salaries of enforcement officials) means that poor-quality medicines could easily be pushed into the formal supply chain of pharmaceuticals:

> If you want your drug to be allowed into the country, if you want your drug to be purchased by a national program, if you want those things to happen, there is a lot of corruption in that. (STK26NG_INGO20150409)

Finally, both categories referred to Chinese vested interests in Laos as a challenge for the efficient management of the quality of medicines circulating in the country. Some reported that foreign-run hospitals bring in their own medicines and escape any form of official controls in doing so – leaving room for a parallel supply chain of potentially poor-quality products.

7.3.3 Economic Frame

7.3.3.1 Economic development and poverty

Government-level respondents referred to issues of economic disparity between Laos and its neighbours, as well as the repercussions on infrastructure development and poverty in the country. This, they argued, impedes the country's capacity to trade equally with its neighbours and to benefit from harmonization efforts. Respondents noted structural challenges to effective drug regulation, including economic disparity between urban and rural areas of the country, high rates of poverty, and the lack of resources at the government level. These structural challenges have impeded the government's ability to enforce the ban on oAMTs, particularly in the more remote mountainous areas of the country where road access and general health infrastructure is poor. High rates of poverty among communities living in rural mountainous areas of Laos also affects health seeking practices; creating a demand for cheaper medicines which tentatively fuels the trade in poor-quality medicines.

Additionally, the slow economic development of Laos, some have argued, leads to limited budget available to finance pharmaceutical regulators (STK21G_NRA20150408). This theme was echoed by a respondent from an implementing partner organization:

> One of the serious limitations for this region, particularly with Laos [is that] they just don't have budget. So, there is a lot of work that doesn't happen. [STK26NG_INGO20150409]

It was interesting to note that, towards the end of the interviews, various respondents asked me for recommendations as to how to obtain funding to support post-marketing surveillance activities or to train current staff members.

Other government respondents mentioned that access to quality medicines also suffers from Laos' position as a 'small market' for medicines on the global scale. Pharmaceutical companies, they argued, do not have an incentive to register their new products in Laos:

> [T]he market is small… many big [pharmaceutical] companies are not interested in registering their [health] products here in the country [Laos]. (STK25G_NRA20150508)

7.3.3.2   Regional investments and inequity

Both government and non-government respondents argued that the changing landscape of investments in the region is a complicating factor for Laos. The number of development projects in Laos, and the mobile migrant workers coming into Laos to support these projects, complicates the task of regulating against poor-quality medicines. Some MMPs, they added, might bring their own medicines, some of which could be of poor-quality.

> We now have a problem of falsified antimalarial drugs because of migration and project investments – especially in the agricultural and mining sectors. (STK30G_MoH20150410)

Both government and non-government representatives argued that Laos is still trying to catch up with the level of infrastructure development in the region, to match its neighbours as equal partners. Respondents explained that Laos is still in the opening phase of market economy which was established in 1986, and that its pharmaceutical sector is weaker that its neighbours. In terms of pharmaceutical production capacity, Laos only has six manufacturing sites, some of which are controlled by the government and are poorly-funded. Additionally, respondents explained that Laos cannot compete as a pharmaceutical export country without adequate GMP certifications in place:

> There are various ASEAN level discussions on manufacturing issues but Lao is not a main producer, it is not easy to talk to other countries who are more advanced in terms of manufacturing. (STK29G_NRA20150410)

For this reason, they argue, the MoH focuses primarily on improving GMP standards, perhaps at the expense of post-marketing surveillance efforts. Government respondents also expressed

concern at the growing ASEAN Economic Community (2015), which may result in increasing exchanges in goods and people in the region and negatively affect less developed countries such as Laos (STK30G_MoH20150410).

Many government respondents also referred to the perceived threat of China: both in terms of the trafficking of illegal products including poor-quality medicines, or APIs from China; and in terms of the investments and money laundering activities by Chinese businesses in Laos. Respondents expressed fear of unbalanced economic investments as a threat to Laos. A law enforcement official further explained that it is likely that Chinese businesses smuggle poor-quality medicines into Laos, through newly built private hospitals in the North of the country.

> Many Chinese businessmen migrate to Lao and do business here, legally and illegally. They may import such kinds of medicines because recently the government policy is to allow private sector investment as private hospitals. (STK27G_LEA20150409)

One official added that such investments are common in the Northern provinces of Laos, where Chinese-run hospitals tend to bring in their medicines from China without registration, with no appropriately translated labels and no quality controls (STK30). The role of China in Laos, as well as the movement of funds either in the form of development projects or money laundering in the region, is perceived to be a threat to Laos and a challenge to guaranteeing access to good-quality medicines. Most themes falling under the economic frame were expanded on further under the Security Frame, as detailed in the next section.

7.3.4 Security Frame

7.3.4.1 The risks of Laos as a transit country

Under the Security Frame, both government and non-government respondents argued that Laos' geographic position and landscape, placed Laos at a high risk from the smuggling of illegal products, including poor-quality medicines. One respondent from the government stated:

> Laos is a landlocked country with border with China, and Vietnam and Myanmar so poor-quality medicines can come in at any point. (STK37G_NCMP20150413)

A respondent from an implementing partner organization confirmed that Laos is in fact prone to smuggling of illegal goods including narcotics – such as opium – but also to the illegal trafficking of wildlife:

> Laos is a hub for illegal wildlife, tiger bones all of that, it is an environment where things that are incredibly illegal in other countries and heavily watched there, it can still exist and flourish here because there is no control. (STK26NG_INGO20150409)

A respondent from the FDD explained that it is therefore common for pharmaceutical products including poor-quality medicines to come in from other countries in the region into Laos unnoticed:

> Pharmaceutical products (fakes or not) can enter the country hidden within other merchandise in big trucks. (STK29G_NRA20150410)

Respondents added that the length of Laos' borders makes it particularly difficult to enforce border control at all entry points, with a respondent from the MoH stating:

> As our territory is very long with borders with the five neighbouring countries and many ports of entry where people and travel / migrate, such medicines can be hidden from the authority and easily cross the border. Our inspectors cannot inspect everywhere, every time. (STK30G_MoH20150410)

Besides the geographical aspect of Lao's position in the region, respondents referred to its neighbouring countries as representing a potential threat to the delivery of quality health services and commodities in Laos.

7.3.4.2   Threat from the region

In their discourse, government-level respondents referred to Laos as a 'victim' amongst its neighbouring countries. Besides alluding to the fact that Laos might be 'lagging behind' in terms of economic development in the region, some portrayed Laos as an 'underdog' facing disproportionate risks and challenges that it does not have the capacity or capability to address, thus placing the country at greater risk of the smuggling of illegal goods. Respondents also referred to the risks posed by neighbouring countries whose regulatory frameworks might differ from that of Laos, leading to the risk of unregistered AMLs infiltrating into Laos from Myanmar:

Poor-quality medicines cannot be stopped from reaching the private sector. The reasons for this are: the borders and the different policies in other countries. (STK24G_NRA20150508)

This overflow into the Laos market, respondents argued, makes it difficult to discern good from poor-quality medicines. More specifically, respondents referred to the growing trade in the region – the increasing movement of goods and people – as a threat for Laos. They argued that the influx of goods of all kinds makes it difficult for regulators to pick out the illegal goods. One respondent from the BFDI asserted that more free trade means a greater risk of increased circulation of illegal products into Laos.

I don't know how we are going to make it, because free movement in terms of medicines for Laos I think… we are not at that level of competition. (STK31NG_IGO20150410)

Respondents argued that the lower economic development status of Laos in relation to its neighbours and the fact that the government is ill-equipped to regulate the influx of trade, creates an exploitable gap for the circulation of poor-quality medicine.

The threat of poor-quality medicines is exacerbated, government-level respondents noted, by the position of Laos in the Mekong region. In this regard, respondents also acknowledged the need for cross border cooperation to deal with this treat. Government respondents mentioned, for example, that cooperation with China would be crucial but note reluctance from their Chinese counterparts to do so, suggesting that the Chinese response is to encourage Laos to control their borders better. Other government respondents argued that cooperation between neighbouring countries through ASEAN for example is crucial to address the threat of poor-quality medicines and harmonize regulatory efforts for pharmaceuticals:

[There are] many benefits from ASEAN cooperation – there is a common standard / technical dossier. It is a platform for knowledge sharing and harmonizing efforts within ASEAN. ASEAN is the only one organization with the capacity for people to survive. (STK20)

A law enforcement representative added that there are also common working guidelines for border control through the ASEAN Agreement on Customs (2012), which encourage all counterparts from ASEAN nations to meet twice a year (STK26). This mechanism, the respondent argued, could provide crucial support to border control efforts in Laos. On the other hand, many respondents also argued that ASEAN cooperation has been slow to date, with

certain countries slowing down the process. The same customs representative explained the challenge of cooperating with their Thai counterparts:

> On cooperation with Thai border towards a single stop inspection, Thai law at the moment is slowing down the process, while in Lao they are ready to start cooperating. Thai law does not allow Thai customs officials to work outside of Thai soil. (STK27G_LEA20150409)

Other respondents explained that, in practice, cooperation is difficult, with some countries such as China refusing to cooperate on tracking or tracing uncovered poor-quality medicines, for example. Another respondent mentioned that varying political priorities across countries makes cross-border cooperation a challenge:

> In practice cooperation across borders is hard, countries do not have the same politics in general (not just on drug management), and there is also a language barrier. (STK34NG_Academia20150410)

Government respondents, while being adamant about the benefits of more regional cooperation on the regulation of pharmaceuticals, were sceptical about the current state of cooperation efforts. Some highlighted the lack of benefits of such cooperative efforts for Laos to date. The fact that Laos is 'lagging behind', government respondents argued, is also a challenge for the harmonization of regulatory frameworks among ASEAN countries. An official stated:

> Our country is a new member of ASEAN and in terms of socio-economic development it still lags behind in comparison to the old member state countries. (STK30G_MoH20150410)

Another respondent from the BFDI expressed concern with regards to the harmonization of registration procedures:

> How to harmonize the registered products for example… that seems a bigger challenge for us. (STK23G_NRA20150508)

This same respondent further explained that, so far, ASEAN and INTERPOL meetings attended by the agency have not brought much change or support to Laos' inspection efforts.

7.3.5 Medical Frame

Few respondents framed the problem of poor-quality medicines in Laos as a medical issue. The only few references that fit under this frame, among government level respondents, were concerns of rising resistance to artemisinin exacerbated by the circulation of Oral Artemisinin Monotherapies. Various respondents expressed concern towards the weak enforcement of the ban on oAMTs:

> Counterfeit and substandard medicines have reduced. We are now fighting oral monotherapy – which is banned, but can still be found.
> (STK24G_NRA20150508)

Respondents also expressed concerns at the irrational use of medicines in general. Most of these arguments, however, were framed more as a health systems issue, as will be detailed in the next section. Respondents argued that the irrational use of medicines is driven, first and foremost, by poor distribution practices and poor accessibility to good quality medicines in remote parts of the country.

7.3.6 Health Systems Frame

Under this frame, both non-government and government level respondents alluded to the health system infrastructure and the poor organization of people and resources to deliver health services to meet the population's health needs.

7.3.6.1 Access to medicine

Both government and non-government respondents explained that patchy access to quality medicines in Laos is due to a weak supply chain of medicines. These challenges to accessibility potentially fuels the trade in poor-quality medicines through unlicensed or mobile itinerant vendors. It is argued that stock-outs of AMLs are an issue, as well as unregistered and substandard. This, they added, is linked to the weak application of licensing requirements and poor reporting methodology. A government respondent, working closely on the malaria program, argued that the distribution of AMLs is suboptimal, especially in the more remote areas of the country:

> [It is] easy [to oversee the distribution of medicines] from the government to the central to the district, but not easy to [do so at] the health centre and village [level]. Our supply chain has some issues; in the health centre, they are far away.

> Sometimes we have reports of stock outs. This is a big challenge for us. (STK37G_NCMP20150413)

Additionally, reporting systems for quantification purposes and to prevent stock-outs are not operated efficiently. Stock-outs are considered very common in remote villages. One government-level respondent mentioned that guaranteeing access to quality medicines in villages in rural areas of the mountainous parts of Laos, is a challenge due to poor road systems. This is especially true, they noted, during the monsoon season when torrential rains make the roads impassable. These same communities are also the least aware of the risks posed by those medicines; either because of a lack of information altogether, because of higher illiteracy rates or because of a language barrier:

> In rural remote areas where there are [different] ethnicities, where people are illiterate, where people do not read Lao you see. We have to do something that can access [reach] them in their dialect, in the language of these ethnicities [ethnic groups]. (STK36NG_Academia20150413)

The problem of poor-quality medicines seems to affect the poorer, vulnerable populations first and foremost. A respondent from the BFDI posed the question:

> [P]eople in remote areas…how do we care for them if they are encountering poor-quality medicines? (STK23G_NRA20150508)

Additionally, accessibility is hindered by the fact that most wholesalers are in or around Vientiane and are often too far from rural villages to guarantee a continuous supply of good-quality medicines:

> In the Southern provinces of Laos, therefore, the big pharmacies (which are mainly in Vientiane Capital) are too far to reach as so it is easier to get medicines from other side of the border or from mobile merchants. (STK34NG_Academia20150410)

Pharmacies near the border, respondents argued, may find it easier to purchase their medicines from unlicensed distributors or from mobile drug vendors. Respondents here referred to situational factors and more specifically to Laos' position as a transit country in the region, increasing instances of smuggling of all kinds of illicit products, including of poor-quality medicines produced in neighbouring countries with greater pharmaceutical production capacity.

This theme bridges onto the medical frame, whereby respondents explained that patchy access to medicine due to poor infrastructure may also lead to the irrational use of medicines and potentially fuel the trade in poor-quality medicines.

> It is like for antibiotics, sometimes people don't take a full dose, or maybe they take a fake, but we don't know yet. (STK37G_NCMP20150413)

Other respondents added that MMPs working on hydro-dams, rubber plantations or other development projects in Laos may also lack adequate access to the right medicines or to health services in general. These workers may therefore bring their own drugs, thereby encouraging the irrational use of medicines.

7.3.6.2   Distribution practices and unlicensed outlets

Non-government respondents referred to the problem of medicine distribution and dispensing practices specifically. They argued that challenges in medicine distribution contribute to the irrational use of medicines and possibly to the circulation of poor-quality medicines. Respondents reported that unlicensed pharmacies and health providers still proliferate in rural parts of Laos, thereby complicating patients' access to quality-assured medicines. The high number of unlicensed outlets, they argued, is partly due to the lack of enforcement of licensing procedures. Respondents explained that while pharmacies outside the PPM scheme are not allowed to sell AMLs, some of them still do. A government official admitted that some unregistered private sector outlets have been found to sell unauthorized oAMTs, including poor-quality ones (STK30G_MoH20150410). A respondent from academia further explained that while pharmacists apply for a license for their pharmaceutical outlets, those are sometimes operated by a relative or friend who does not necessarily possess the correct qualifications (STK34NG_Academia20150410). Other respondents added that there exist unlicensed foreign pharmacies for the Vietnamese or Chinese communities in Laos selling their own pharmaceutical products, most of which are not registered in Laos. These unlicensed vendors, respondents noted, could provide an outlet for poor-quality medicines that escape inspection. This may in turn contribute to the irrational use of medicines and fuel the trade in poor-quality medicines.

One non-government respondent from an implementing partner organization argued that pharmacists in Laos tend to buy left-over medicines from individuals such as tourists, to complete their stock and have more to offer to their clients, without concern for the source or expiration dates of those medicines (STK26NG_INGO20150409). This respondent implied

that pharmacies operated by untrained professionals may be tempted to purchase cheaper stocks from mobile itinerant vendors (STK26NG_INGO20150409). Such medicines are thereafter inappropriately distributed to patients. Additionally, the fact that prescription requirements are rarely followed was perceived as another challenge by non-government respondents.

> [T]here is no such thing as a prescription medicine here, so maybe that's another problem because we don't have tight controls on who can get what product, you just go to a pharmacy and ask for what you want. (STK26NG_INGO20150409)

Finally, another challenge identified is the distribution of medicines as cocktails of drugs or '*yaa chud*' as they are referred to in Laos. In such packages, it is not uncommon to find a mix of drugs including anti-infective in the wrong dosage or poor-quality medicines. Such practices, it is perceived, not only perpetuate the irrational use of medicines, but could create an opportunity for the sale of poor-quality medicines without the possibility to trace them back to their source.

7.4   Frames and the policy process

A few observations can be made on how the problem of poor-quality medicines is framed by policy actors in Laos and their implications for policy making in this country. The results suggest that poor-quality medicines are still perceived as a challenge for Laos. Although there is evidence that falsified AMLs are no longer the main concern, it is believed that substandard AMLs and other essential medicines remain a threat. One key observation is actors' openness to evidence-based policy making, with policy makers demonstrating strong links with the LOMWRU team, for example.

The common thread between the dominant themes from the semi-structured interviews is an emphasis on uneven development and economic disparities within the region. Respondents shared a common perception of Laos as the 'underdog' of the Mekong region. In this regard, respondents also defended the value of external aid and international development support to its pharmaceutical regulatory framework. Most government-level respondents concurred that ASEAN regional harmonization efforts would provide undeniable support for Laos' drug regulatory authority and alleviate pressure on its pre-marketing regulatory efforts. This openness to regional harmonization efforts and to external support, echoes Phase I of the policy process and is a legacy of international aid efforts to build Laos' health systems from 1993 onwards. Some government representatives expressed concern as to what appears to be a

catch-22 situation, stating that despite the encouraging news that Laos' GDP is on the rise, once it reaches a certain threshold, the country will no longer be eligible for all types of external funding which might hinder drug quality monitoring efforts.

One clear policy challenge to the effective enforcement of rules and regulations, is the vested interests of regional investors, including Chinese business owners in the North of Laos. Government-level respondents explained that inspections are rarely conducted on privately owned hospitals run by foreign nationals – including Chinese businessmen. This suggests a parallel health delivery system and supply chain of medicines that escape quality control or any other form of official regulation, leaving room for the infiltration of unauthorized, unregistered, and even substandard or falsified pharmaceutical products. This is testimony to a lack of transparency in the health system and in the regulation of medicines. We have yet to observe whether the 2012 Law on Making Legislation, introduced to encourage more transparency in policy making, will have repercussions on fair implementation of existing regulations to monitor drug quality.

Results suggest a strong awareness among policy makers of the threat of poor-quality medicines for infectious disease control in Laos and beyond. Government respondents demonstrated a willingness to resolve this challenge through joint cross-sectoral and cross-border efforts. The results suggest that the majority of government respondents involved in the regulation of pharmaceutical are committed to the fight against poor-quality medicines. Most government respondents, as noted earlier, demonstrated a thorough awareness of existing rules and regulations.

Most non-government respondents argued, however, that there is still a lack of concrete political commitment to this aim among government-level agencies. While the current regulatory framework strongly encourages international cooperation for the exchange of expertise and information, as well as cross-sectoral cooperation between government agencies, no policy document proposes a mechanism institutionalizing cooperation to support efforts against counterfeit, falsified or substandard medicines. Results suggest a lack of a strong policy subsystem to facilitate cross-sectoral cooperation against poor-quality medicines. It appears that, besides the network LOWMRU as an epistemic network of knowledge sharing informing policy making, there is no other systematic network in place in Laos to facilitate cross-sectoral cooperation. This arguably translates into limited accountability towards the policy problem of poor-quality medicines. Instead, government-level officials emphasized the need to cooperate across-borders to address a challenge that was essentially a regional problem.

Policy actors also argued that considering the weak capacity to enforce the current regulatory framework, the government's priority is first to secure the supply chain of medicines so as to reduce the number of unregistered and substandard medicines, before engaging in post-marketing surveillance activities to track and trace falsified medicines. This corresponds with the emphasis on drug safety and efficacy throughout the policy development process, and the more recent focus on tackling the problem of substandard medicines and of oAMTs. Despite the recognition of the threat of *falsified* medicines by respondents, there are few concrete mechanisms against the crime of medicine falsification. The FDD explains that, in light of the challenges to *accessibility* resulting from inequitable growth, the priority for the government is first to strengthen supply chain management and to prevent the irrational use of medicines.

Chapter 8   Thailand

8.1   Background

Figure 15 Map of Thailand (Source: United Nations Map available at www.un.org)

Thailand, officially known as Siam until 1949 and thereafter as the Kingdom of Thailand, has never endured the oppression of a colonized power, in contrast to its Southeast Asian neighbours (Strate 2015). The country switched from an absolute monarchy to a constitutional monarchy following the 1932 democracy revolution (Connors 2003). Following this revolution, Thailand was predominantly ruled by military dictatorships (Baker & Phongpaichit 2014). Since the establishment of the constitutional monarchy, there have been 8 coup d'états and 20 constitutions. In 2014, the military took power and proposed a referendum on a new constitution, for which the population voted in favour in August 2016 (BBC 2016). The political climate in Thailand, however, remains tense and unstable (Chachavalpongpun 2015).

As illustrated in the map above (Figure 15 page 182), the Mekong River follows the Thai-Lao border along the north-east of the country. The border between Thailand and Burma has been

regularly closed to traffic due to clashes with rebel insurgents (Ganesan 2015), while relations between Cambodia and Thailand have been strained since 2008 over the Preah Vihear temple dispute in the East – where both countries claim the territory and historical heritage, despite an international court of justice decision in 1962 ruling that the temple (a World Heritage Site) belonged to Cambodia (St John 1994). The capital City of Bangkok is surrounded by 76 provinces which are geographically grouped into 6 regions and are subdivided into 877 districts (Bureau of Vector Borne Diseases 2011). The Thai population is largely homogenous, with 96% of Thai ethnicity and the remainder 4% including minority communities of Chinese, Mala and Khmer origin, as well as Hill Tribe populations (Pongpisut *et al.* 2015). The International Organization for Migration in Bangkok estimates the presence of approximately 1.8 million registered migrants and between 1.8 and 4 million irregular migrants, with up to 80% from Myanmar, 10% from Cambodia and the rest mainly from Laos (STK54NG_INGO20150910).

Indicator	Value	Year (Source)
Total Population (million)	68	2015 (WB)
Gross Domestic Product – Purchasing Power Parity (International $)	16,305	2015 (WB)
Human Development Index	0.726 (Rank 93)	2014 (UNDP)

Table 15 Thailand economic and development indicators

Thailand has been a member of the Asian Development Bank (ADB) since 1966, and a member of the Association of Southeast Asian Nations (ASEAN) since its inception in 1967. It is part of the World Health Organization (WHO) South East Asian Regional Office (SEARO), headquartered in New Delhi. Despite political instability, Thailand has experienced rapid economic development[40] through various stages of recovery and re-growth. Poverty rates have reduced from 67% to 11% between 1986 to 2014 (WB 2015). Challenges to economic growth have included regional economic crises, political tensions, inequality and an ageing population (ADB 2015). The 1997 Asian financial crisis, for example, had a considerable impact on the Thai economy, as the Thai Baht fell sharply leading to high rates of unemployment (International Monetary Fund 2000). The 2008 global economic crisis also led to uneven economic growth in subsequent years. The average growth rate was at 7.5% in the 1980s and 1990s (WB 2015). While the growth rate was forecasted at 7%, for 2016 it was only

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[40] Thailand is categorized as an Upper Middle Income Country by the World Bank since 2011.

3.2% (ADB 2017). Thailand's economy is driven predominantly by the mining of natural resources in the mountainous areas of the north and tourism in the south, while the north relies considerably on manual labour by migrant workers.

Thailand also has a strong pharmaceutical sector with over 172 local manufacturers. The domestic pharmaceutical industry in Thailand grew rapidly since 1943 when the Thai Government Pharmaceutical Organization (GPO), a state enterprise that manufactures and supplies affordable generic medicines for the Thai government and directly to public hospitals, was established. By 2013, the value of the drug market was estimated at 4.5 billion US$ (PharmaBoardroom 2015). Due to its strong generic production industry, Thailand has previously made use of Compulsory Licensing as a flexibility clause to the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), to bypass patent laws and locally produce more affordable alternatives to expensive medicines. This was the case in 2007, when Thailand entered in a dispute with Abbott pharmaceuticals over the compulsory licensing of an HIV Drug, Kaletra (Steinbrook 2007). The value of imported medicines, however, remains higher than that of locally-produced medicines, as over 650 different types of medicines are still imported into the country. Another growing strength of the Thai health sector is the number of private sector providers and for-profit hospitals (Teerawattananon *et al.* 2003).

8.1.1   Thai health sector

Indicator	Value	Year (source)
Total Health Expenditure (% of GDP)	6.5	2014 (WB)
Health Expenditure Per Capita (Current US$)	360	2014 (WB)
Out-of-pocket Health Expenditure (% of Total Health Expenditure)	7.9	2014 (WB)
Physicians per 1,000 population	0.4	2010 (WB)
Pharmacists per 1,000 population	0.12	2004 (Thai Health Resource Survey)
Life Expectancy	74.4	(WB)

Table 16 Thailand health indicators

The public health sector has grown steadily since the establishment of the Thai Ministry of Public Health (MoPH) in 1942. By 1956, every province had a hospital with a referral centre (Thaworn 2015). Public hospitals now represent between 75 and 79% of all hospital beds in Thailand (Pongpisut *et al.* 2015). The first focus of the health sector reforms in the 1980s, was to invest in the infrastructure of health facilities in rural areas (Pongpisut *et al.* 2015). Subsequently, reforms addressed health financing and social security schemes[41]. Coverage of all health insurance funds went from 92.48% in 2002 to 97% by 2007 (Thaworn 2015). Registered migrant workers are also included in the social security schemes and have access to health facilities in Thailand. Universal health coverage (UHC) in Thailand was achieved by 2002 with the 30 baht scheme[42] (Pongpisut *et al.* 2015). This system has worked to increase access to health for the poor and reduce mortality rates (Gruber *et al.* 2014). Mortality rates in Thailand have been declining since the 1980s. The main causes of mortality since the end of the 20th century have been non-communicable diseases (NCDs), although HIV/AIDS and tuberculosis still largely contribute to the Thai health burden (Bundhamcharoen *et al.* 2011) along with an ageing population (UNDP 2011). To address these health challenges, the Thai government continues to invest in its public health sector at 6.4% of its Gross Domestic Product (WB 2014). Per capita total expenditure on health is above the WHO SEARO regional average. Out-of-pocket payments have considerably reduced at 7.9% of THE in 2014, compared to 44.5% in 1994 (WB 2014).

8.1.2   Regulating antimalarial medicines in Thailand

The main law regulating pharmaceuticals in Thailand is the Drug Act B.E. 2510 (1967) which outlines the regulation for pre-marketing authorization, licensing as well as post-marketing surveillance. This Act has been revised four times since 1967 – the latest revision dating back to 1987. Appendix 17 Page 380 summarizes the results of my analysis of the Act, its amendments and one other policy document relating to the regulation of pharmaceuticals in Thailand. The MoPH is responsible for the health sector including the regulation of health

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[41] There are three Social Security Schemes available to support Universal Health Coverage in Thailand, including the Social Security Scheme for employed staff, the Civil Servant Medical Benefit Scheme funded by the Ministry of Finance and the Compulsory Migrant Health Insurance Scheme. Uptake of the latter is unknown but is estimated at 4 million, amongst those migrants who possess a work permit. Most social security schemes, however, only cover essential medicines (available for free) and reach out to an estimated 74% of the population (Holloway 2012).

[42] Registered users, including registered migrant workers, contribute a flat fee of 30 Thai Baht (60p) per consultation to access public health services (Coronini-Cronberg *et al.* 2007).

products[43], and consists of four main clusters as illustrated in Figure 16 (page 189). Under the Cluster of Public Health Development, and the Cluster of Public Health Services Support, three departments are involved in the control of medicine quality; namely the Department of Disease Control (DDC) the Department of Medical Sciences (DMS), and the Thai Food and Drug Administration (TFDA).

The process of decentralization of the public health sector since the late 1990s, provides an opportunity for the MoPH to improve oversight over the pharmaceutical sector and supply chain in more remote parts of the country. Below the central level of the MoPH in Nonthaburi are the regional health offices, the provincial public health offices (PPHOs), the district health offices, and the health centres. The 1999 Decentralization Act called for decision-making powers, as well as financial powers to be delegated to PPHOs. The TFDA (previously named Food & Drug Division) was established in 1937 as the drug regulatory authority, to monitor the efficacy and quality of health products in Thailand. The TFDA is the main actor raising awareness and harnessing expertise across MoPH departments to improve access to quality essential medicines in Thailand. The central TFDA delegates many aspects of pharmaceutical regulation to the PPHOs such as the licensing of manufacturers, and works with its provincial counterparts in monitoring the quality of medicines. Since 2003, the TFDA is made up of 10 divisions summarized in Table 17 below (page 187). The Drug Control Division (DCD) of the TFDA is responsible for pre- and post-marketing regulatory functions. For more information on Thailand's pharmaceutical regulatory system, refer to Appendix 15 on page 369.

Health Product Control Division Group	Support Division Group
Bureuau of Cosmetic and Hazardous Substances Control	Public and Consumer Affairs Division
Drug Control Division	Rural and Local Consumer Health Products Protection and Promotion Division
Food Control Division	Technical and Planning Division
Medical Devices Control Division	Office of the Secretary
Narcotics Control Division	
Import and Export Inspection Division	

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[43] The policy actors present in the pharmaceutical regulatory space in Thailand are summarized in Appendix 16 Page 373.

Table 17 Structure of the Thai Food and Drug Administration

The Malaria Program is managed by the Malaria Cluster of the Bureau of Vector Borne Diseases (BVBD), located within the MoPH's Department of Disease Control (DDC). The Program has been funded by the Thai government and the Global Fund (GF) since 2004. The BVBD oversees the procurement and distribution of AMLs, through a parallel system. AMLs are purchased through manufacturers, including the GPO. Most AMLs are purchased through the government budget (4-5 million baht each year), while the rest are procured through the voluntary pooled procurement mechanism of the Global Fund (GF) and destined mainly to non-governmental organizations, or migrant camps in border areas (STK40G_NMCP20150603). Figure 17 (page 190) shows that malaria treatments are procured and supplied differently for malaria posts (MPs) or clinics (MCs) (Thumm 2009). Since 1995, AMLs are under strict distribution control aimed at minimizing the irrational use of AMLs, and it is therefore illegal for private sector outlets to dispense AMLs. BVBD cooperates with the Bureau of Drugs and Narcotics (BDN) under the DMS on sample testing for the quality control of AMLs.

Malaria incidence rates in Thailand have considerably reduced to meet the Millennium Development Goal of a 75% incidence rate reduction target between 2000 and 2015. In Thailand, malaria is also a forest-related disease found predominantly in border areas, and more specifically along the Thai-Burmese, Thai-Cambodian and Thai-Malaysian borders (Thumm 2009; Bureau of Vector Borne Diseases 2011). Both *Plasmodium falciparum* (42%) and *Plasmodium vivax* (58%) can be found in Thailand. Malaria remains a burden predominantly among Mobile Migrant Populations (MMPs) (Bhumiratana *et al.* 2013) and 8% of population are reported as still living in high transmission areas. The reported number of cases in 2015 was 24,850 (MEI UCSF 2016), while the estimated total number of cases is double that amount. Thailand is nevertheless on track for malaria elimination to meet a 2024 national target, and participates in efforts to reduce the risks of antimicrobial resistance (Thai National Malaria Elimination Strategy 2017-2026). Possible challenges to elimination in border areas include artemisinin resistance, particularly at the Thai-Cambodian border – the same area where resistance to mefloquine was first spotted in the 1990s (Bhumiratana *et al.* 2013; Thumm 2009). The BVBD acknowledges the presence of markers of artemisinin resistance in 6 border provinces and, as a result, treatment recommendations change regularly in line with emerging resistance to artemisinin. ACTs were introduced in 1998 and the current recommended first line treatment for malaria recently changed to DHA Priperaquine, instead

of Mefloquine and Primaquine. Second line treatments include Quinine and tetracycline, and third line treatments include artesunate and artemether.
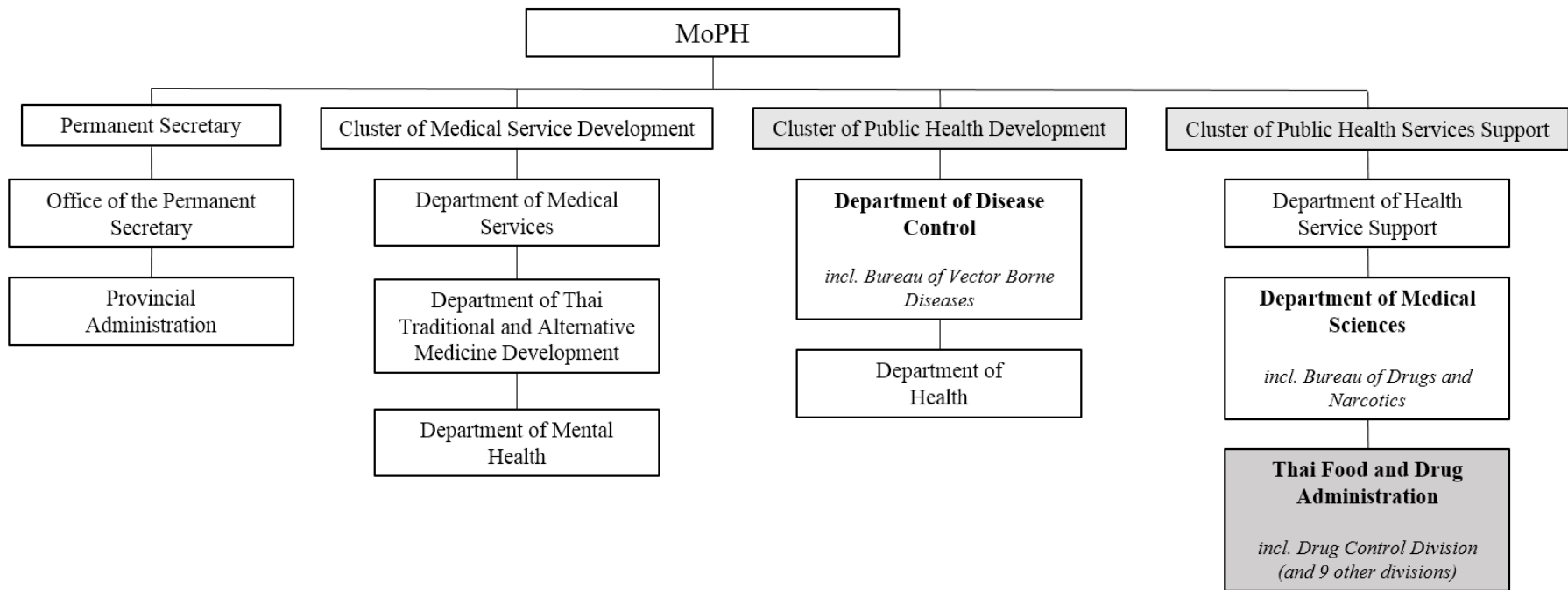
Figure 16 Overview of Ministry of Public Health structure
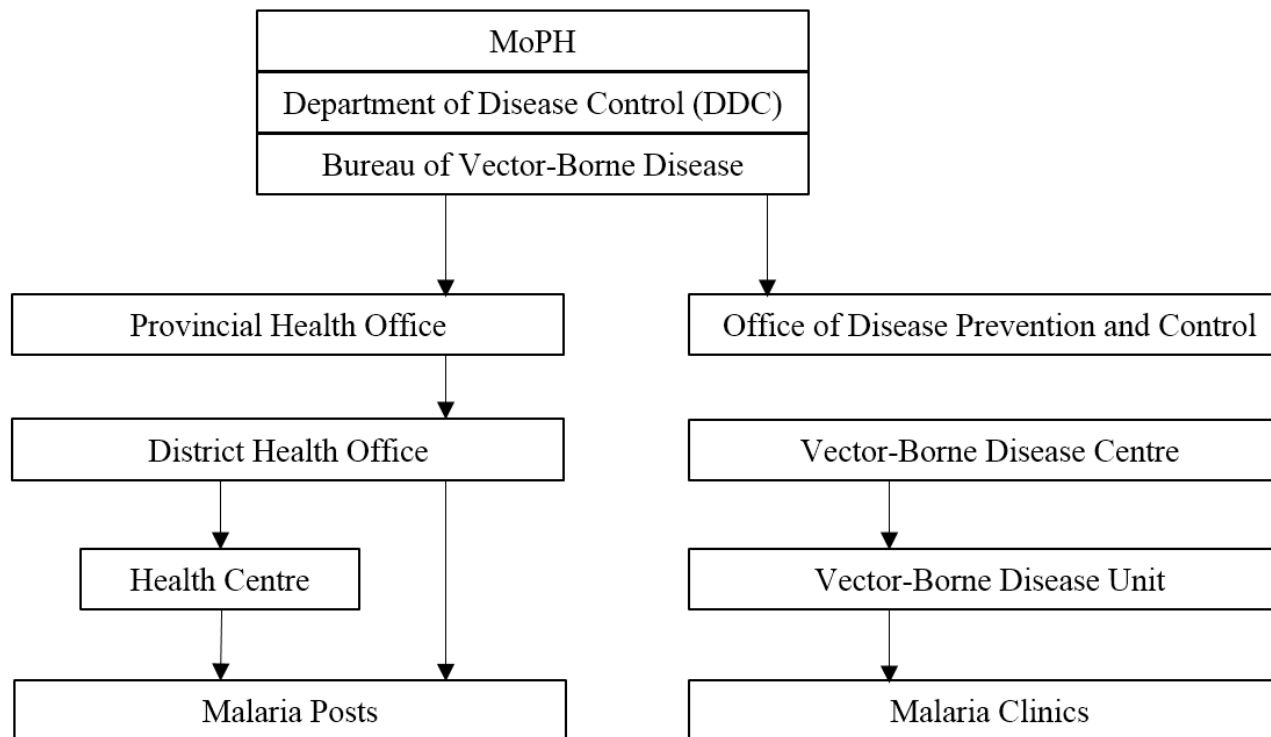
Figure 17 Public sector malaria services and supply system (Thumm 2009)

8.2   Policy developments against poor-quality AMLs

From my analysis, I discern four phases of policy around regulating the quality of medicines. These four phases stretch over a period of 80 years since the establishment of the TFDA. The first phase sees an initial emphasis on consumer protection from inefficacious medicines and on the protection of trade interests for a rapidly growing domestic pharmaceutical industry. In the second phase, the focus of regulatory efforts is on improving access to health services in general, with an emphasis on establishing a stronger social security system towards Universal Health Coverage. This is perceived as one tangible effort to reducing the demand for cheaper medicines from unlicensed outlets that may contribute to drug resistant malaria. The third phase marks a turning point, with the drafting of a New Drug Act aimed in part at improving penalties against the production, sale and distribution of poor-quality medicines. With the process of promulgation of the New Act coming to a stall, the government switched its attention in the fourth phase of the policy process to strengthening the pharmacovigilance (PV) system. The timeline available on page 192 (Figure 18) provides a chronological overview of the laws and policies introduced over time to regulate pharmaceuticals and their quality in Thailand.
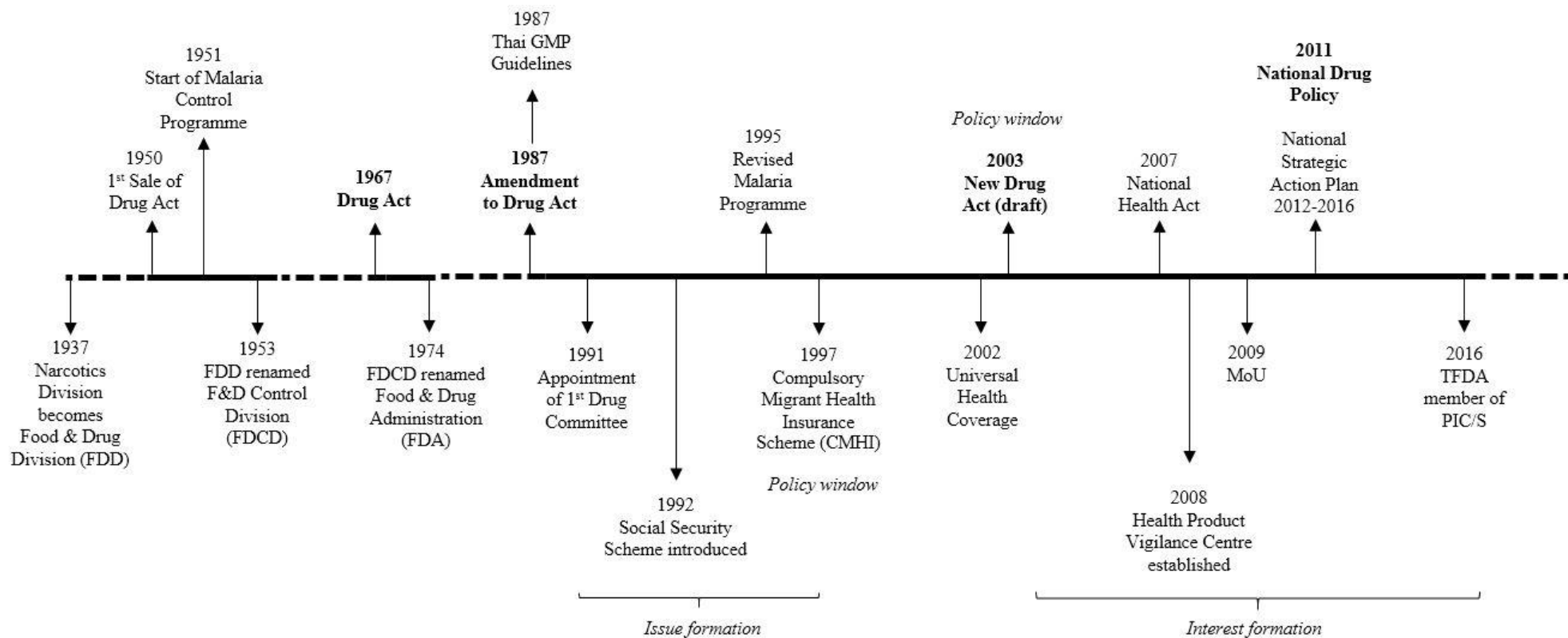
Figure 18 Timeline of policy developments for pharmaceutical regulation in Thailand

8.2.1 Phase I: Trade and the Thai pharmaceutical sector (1937-1997)

8.2.1.1 Consumer protection and pharmaceutical efficacy

The language used to outline the mission of the TFDA and The Drug Act also places most emphasis on consumer protection, drug safety and efficacy[44]. The Drug Act states, for example, that all drugs that are not 'scientifically efficacious' will be withdrawn from the market. At this initial stage in the regulation of pharmaceuticals, the problem of poor-quality medicines is perceived as a problem only in so far as medicines do not fulfil their medical purpose, therefore putting patients at risk of Adverse Drug Reactions (ADR). The definition of poor-quality medicines in the Drug Act 1967, as well as in the 1987 amendment (Drug Act B.E. 2530, 1987) uses neither the term 'counterfeit' nor 'falsified', but instead refers to 'fake' 'deteriorated' or 'substandard' medicines. This definition focuses predominantly on the lack of medical efficacy of the drug rather than the criminal intent of medicines falsification. It does not make a distinction between poor-quality drugs manufactured with the *intent* to deceive and drugs that are substandard because of manufacturing errors. The definition is predominantly focused on the sub-optimal characteristics of 'fake' drugs and the medical repercussions for the patient.

The definition of 'fake drug' in Section 74 of the 1967 Drug Act, more specifically, defines a 'fake drug' as one which 'falsely shows it is in accordance with a formula which has been registered' or one 'with active substances which quantity or strength lower that the minimum or higher than the maximum standard' (by more than 20%). The Drug Act adds that if the threshold is less than 20%, it will fall in the category of 'sub-standard drugs' defined in Section 74 as 'drugs produced so that their purity or other characteristics which are important to their quality differ from the standards prescribed in the registered formula…' By defining this efficacy threshold, the definition of a 'fake drug' uses pharmacovigilance language. Additionally, the Drug Act refers to prescription-only medicines, such as antibiotics as 'dangerous drugs'. This choice of terminology suggests a strong focus on the health implications of the irrational use of medicines or sub-standard drugs for consumer health. As Teerawattananon and colleagues (2003) point out, the emphasis on consumer health protection apparent in the 1967 Drug Act is reinforced in the 1997 Thai constitution.

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[44] Appendix 17 page 380 provides an overview of the definition of poor-quality medicines in Thailand from eight legal and policy documents.

This phase of the policy process also marks the start of efforts to control and guarantee the quality of essential medicines for patients. The Drug Act 1967 plans for all new drugs that have successfully passed the registration assessment to receive provisional market authorization (MA) for two years, during which the products are part of a safety-monitoring program (SMP). During the SMP, the drug can only be sold through public health facilities (not pharmacies) and dispensed by medical professionals. Adverse Drug Reactions (ADRs) are monitored closely during this two-year period. If the product's benefits are verified, it will receive an unconditional approval for its distribution through other channels. Secondly, Thailand's National Drug Testing Laboratory[45] (NDTL) was established in 1974. The NDTL received a fixed government budget allocation in support of its activities, which include testing the quality of pharmaceutical products. By 1986, the NDTL was a designated WHO Collaborating Centre for Quality Assurance of Essential Drugs, meaning that it serves as a drug testing facility for essential medicines in the region[46]. The 1967 Drug Act also stipulates penalties against the production and sale of poor-quality medicines[47].

8.2.1.2 Growing Thai pharmaceutical sector

Another main observation in this early phase of the policy process, is the emphasis on pharmaceutical trade and protecting the interests of a growing domestic pharmaceutical industry. The official definition of 'fake drug' encompasses drug counterfeiting and refers directly to brand infringement. Despite not using the term counterfeit, a 'fake drug' is defined as 'an imitation for a genuine drug' or a drug that 'shows the name of another drug' or that 'shows a name or mark of a producer, which is false' (Section 73, Drug Act 1967). The definition of poor-quality medicines in the Drug Act does not differentiate between *counterfeit* or *falsified* medicines with no emphasis on the challenge of pharmaceutical crime. The Drug Acts focus instead on regulating the local generic industry, imports and exports of pharmaceuticals, emphasising on the requirements for Thai manufacturers to get 'up to speed' on the production of affordable, quality and generic medicines fit for export. The Drug Act includes various clauses on registration procedures for generic medicines, which is the biggest share of the pharmaceutical industry in Thailand according to a respondent from the Pharmaceutical Research & Manufacturers Association (PReMA). It provides detailed requirements on the production of pharmaceuticals, such as the testing of raw materials, batch

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[45] The NDTL is hosted by the Bureau of Drugs and Narcotics which is part of the Department of Medical Sciences of the Thai Ministry of Public Health.

[46] The NDTL is ISO 17025 certified since 1994.

[47] In Section 103, the Act states that any pharmacy or drug outlet that does not abide by the terms of the Act – including those stipulated under Chapter 8 with regards to the sale of fake, substandard or deteriorated drugs - shall be liable to a fine of up to 5,000 baht, renewable daily until rectification.

numbering and labelling (Section 25). The TFDA introduced Good Manufacturing Practices (GMP) guidelines[48] in 1987 as an important initiative, contributing to the development of the Thai pharmaceutical industry and promoting the safe local production of quality medicines (Thai Food and Drug Administration n.d.). While focusing on the local generic production of affordable medicines, the Thai government also places much emphasis on patent law. Section 51 of the Patent Act (No. 3) B.E. 2542 (1999), for example, recognizes the right of 'any ministry or department of the Government' to exercise any right conferred by the patent to carry out any service 'for public consumption'. Thailand has previously reached out to the flexibility mechanisms of the TRIPS Agreement, including compulsory licensing[49] and parallel importation, thus promoting access to affordable essential treatments including HIV AIDS treatments (Kuek *et al.* 2010). In parallel, Thailand placed great emphasis on the development of a Thai pharmacopeia, which has become a reference in the region.

8.2.2   Phase II: Access to quality healthcare and essential medicines (1997-2003)

8.2.2.1   The role of evidence

This second phase of the policy process coincides with evidence of chloroquine resistance at the Thai-Cambodia border (Nosten *et al.* 1994). Resistance to chloroquine-based treatments and slower parasite clearance in malaria patients, especially in migrant workers, was perceived as an important challenge to malaria elimination. Shakoor *et al.* (1997) first reported the circulation of poor-quality AMLs in Thailand (and Nigeria), where 40% of chloroquine tablet samples were found to be substandard. Subsequently, Newton and colleagues (2001) report in a region-wide study that 11 % of artesunate tablets samples from Thailand were falsified. In 2002, Newton and colleagues wrote that between 38%-53% of AMLs sampled from pharmacies and shops in Cambodia, Laos, Myanmar, Thailand and Vietnam were counterfeit (Newton *et al.* 2002). Poor access to quality medicines and the circulation of poor-quality ones, was seen to exacerbate the problem of drug-resistant malaria. This evidence served to raise awareness about the patchy access to quality medicines in border areas, as well as the emerging threat of antimicrobial resistance for malaria control (Dondorp *et al.* 2009).

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[48] By 2001, the Thai GMP guidelines were WHO recognized and the TFDA regularly conducts education initiatives to encourage and promote adherence to these guidelines.

[49] Such as for Efavirenz in 2006 or Lopinavir-ritonavir in 2007, both pricey antiretroviral treatments.

8.2.2.2   Improving access to health

The Thai government gradually focused on improving the social security system (including for migrant workers) to improve access to both health services and health commodities, including essential medicines. In 1997, Thailand introduced the Compulsory Migrant Health Insurance Scheme (CMHIS) (or the '30 Baht Scheme') which facilitated access to health services for migrant workers. Universal Health Coverage was fully established by 2002. Additionally, the National Health Security Office (NHSO) established in 2002 by the National Health Security Act 2002, has been a key player in improving access to affordable, quality medicines (WHO SEARO 2013). The NHSO is mandated to operate the pharmaceutical procurement budget for the MoPH (Holloway 2012), allowing all of the medicines on the National Essential Medicines List[50] (NEML) to be available free of charge. The NHSO also runs a vertical procurement system for high priced medicines (96 of them), such as anti-cancer or anti-retroviral treatments. Another key partner in improving *access* to quality medicines for all is the GPO. As detailed in a report by the WHO, the GPO manufactures over 132 drugs on the NEML and supplies approximately 1000 products across Thailand to both public and private facilities, and acts as a pharmaceutical storage facility (Holloway 2012). The role of the GPO is crucial to reduce the price of medicines through economies of scale (Holloway 2012). Its procurement system has contributed to improving access to affordable medicines and improving trust in the public health system, aiming to reduce the tendency for patients to self-medicate and to purchase treatments from unlicensed vendors selling cheaper medicines.

8.2.3   Phase III: The New Drug Act (2003)

8.2.3.1   New evidence: a turning point

New evidence of the circulation of poor-quality antimalarial medicines re-instigated the government's interest in strengthening regulations to secure the supply chain of pharmaceuticals. Studies by Dondorp and colleagues (2004) and Hall and colleagues (2006), for example, reported that between 27% and 35% antimalarials sampled were of poor-quality. Evidence of artemisinin resistance at the Thai-Cambodian border, supposedly aggravated by the irrational use of medicines and the circulation of unregistered or substandard treatments, was recognized as a real threat in this fourth phase of the policy process. 2003 marks a turning point, in which efforts were spurred to strengthen the pharmaceutical regulatory system through, for example, the enforcement of measures against unlicensed online pharmacies.

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[50] This list is revised annually with a panel of 17 experts (Holloway 2012).

Since 2003, the TFDA added two divisions to bring the total to ten. As part of its post-marketing surveillance (PMS) operations, the TFDA is mandated to conduct annual planned inspections of newly established premises (pharmaceutical outlets, warehouses etc.) and follow-up inspections, as well as conduct routine inspections of pharmaceutical product batch samples at ports of entry. TFDA inspectors from the Import and Export Inspection Division are stationed at these ports of entry and work alongside customs officials. In addition, the TFDA conducts inspections on request to investigate suspect cases and to gather information for the administration of legal sanctions.

8.2.3.2 Stalled reforms: The New Drug Act

A New Drug Act (B.E. 2546, 2003) was drafted and aimed to reinforce GMP compliance for manufacturing licenses and increase penalties for the production and sale of substandard and falsified medicines. This New Drug Act, however, remains in the promulgation stage, stalled by a lack of agreement among the various stakeholders involved in pharmaceutical regulation on the content of the document, especially with regards to the penalties incurred for the production, distribution and sale of poor-quality medicines. Its content is currently still being debated at the National Assembly. The first element of controversy around this Act is the proposal that government-owned enterprises or agencies will no longer be exempt from the requirements of licensing and product registration. This shift translates the desire to tighten registration guidelines. Despite noted efforts to combine two proposals in this Act from the public sector and from the industry, respondents alluded to continuous and unsuccessful negotiations regarding its content – between members of the MoPH, civil society, as well as domestic industry representatives.

According to the TFDA website, the New Drug Act plans to considerably increase the penalties[51] for the production, sale and import of fake, substandard or deteriorated drugs to better reflect the severity of the crimes. The revision of the penalties has led to much debate, as confirmed by various respondents from the industry, academia and government institutions, especially over Section 38 of the New Drug Act, which proposes capping the fine and prison time (to 20,000 baht and 5 years) for manufacturers who produce fake drugs that are not 'harmful' to the user. Adding this differentiation between poor-quality drugs that are 'harmful' and those that are 'not harmful' to the consumer, however, is dangerous, as it implies that not all pharmaceutical crimes are as serious. In practice, proving this differentiation may also be

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[51] A summary of penalties incurred is available in Appendix on further information on the Thai pharmaceutical regulatory system (Appendix 15, page 369).

challenging and respondents added that this point causes friction among experts in negotiations for the New Drug Act (2003), especially between industry and government representatives. Despite the policy controversy over the revision of the Drug Act, 2003 marked a shift of focus, with an initial intention to address evidence of circulation of poor-quality medicines. Efforts to increase penalties and strengthen post-marketing surveillance, as well as the penalties for the circulation of poor-quality medicines, have had limited success thus far.

8.2.4 Phase IV: Strengthening pre-marketing and pharmacovigilance (2003-2016)

8.2.4.1 Further evidence of the risks of poor-quality medicines

This fourth phase of the policy process demonstrates a renewed emphasis on strengthening PV activities, potentially in response to reports of ADR across drug categories but also to evidence the irrational use of medicines and the associated risks for artemisinin resistance. Since 2006, there has been a lack of data on prevalence rates for poor-quality AMLs in Thailand, however, some studies suggest that evidence of artemisinin resistance at the Thailand-Cambodia could be related to the continued circulation of poor-quality artesunate (P. Newton et al. 2008). A number of findings across the Mekong Region have drawn increasing attention to the problem of poor-quality AMLs, including in Thailand. Other studies provide evidence of the circulation of different types of poor-quality pharmaceuticals in Thailand, such as Erectile Dysfunction treatments. According to a study in Eastern Thailand conducted by Homhuan (2013), for example, 88% of erectile dysfunction drugs surveyed had a sub-standard API dose. Such evidence prompts general concern about ADR across therapeutic categories. With malaria incidence rates sharply reducing in central Thailand, respondents suggest a shift of attention within the TFDA from malaria control and the surveillance of poor-quality AMLs, towards efforts to strengthen PV for lifestyle medicines and herbal supplements.

8.2.4.2 New mechanisms for post-marketing surveillance

Despite efforts to strengthen pre-marketing and PV efforts, however, reports suggest continuous concern with regards to the smuggling of poor-quality medicines and the need to strengthen post-marketing surveillance (Fotiou *et al.* 2009). Thailand is prone to the online sale of pharmaceuticals through illegal internet pharmacies, for example, exacerbated by the use of social media (such as Facebook) to advertise products (Homhuan 2013). The TFDA estimated that 30 million US$ worth of falsified medicines are sold yearly in Thailand (World Health Professionals Alliance 2011), although the reported percentage of failed sample testing by the Bureau remains low at approximately 5% between 2013 and 2015. The TFDA set up a

Centre for Combating Counterfeit Drugs in 2008, encouraging consumers to provide information about poor-quality medicines to the authorities. This centre is first and foremost an information sharing platform, however, its website has not been updated since its launch. TFDA also publishes the results of its quality assurance inspections annually in a Green Book and hospitals use this book to guide their purchases.

In response to the perceived international threat of smuggling of poor-quality medicines, the Thai government has favoured inter-sectoral cooperation. A Memorandum of Understanding (MoU) was signed in 2009 by nine government agencies including, the TFDA, the Ministry of Information and Communication Technology (MICT), the Ministry of Industry (MoI), the Ministry of Commerce (MoC), but also Customs (CUST), Police (POL), the Association of Pharmaceutical Research and Manufacturers (PReMA), the Department of Special Investigation, the Central Institute of Forensic Science, and the Office of the Attorney General for Intellectual Property Department. The available documents and the interviews conducted in Thailand, however, provided little information on the extent or the nature of collaborations between these nine institutions. Judging from the composition of this lose partnership, the emphasis seems to be first and foremost on protecting the industry interests and tackling the problem of 'counterfeit' medicines, as suggested in the title of the MoU, rather than the challenge of poor-quality medicines at large. Results do, however, suggest that the MICT is involved because of its expertise with website technology through which e-pharmacies sell their products. Customs and police officials and the Police Consumer Protection Unit (CPU) are involved in enforcing the licensing requirements of the TFDA. Customs officials and TFDA inspectors work jointly at border checkpoints to verify the quality of pharmaceutical imports. Industry representatives also actively train customs officials to recognize genuine vs. falsified (or counterfeit) product batches at formal border checkpoints. Arguably, the Ministries of Industry and Commerce are involved in supporting the growth of Thailand's growing pharmaceutical industry by regulating the imports and export of pharmaceutical products.

8.2.4.3   Cross-sectoral collaboration

As partly demonstrated by the mechanisms described above, the particularity of the Thai policy development process is the inclusion of representatives from the pharmaceutical sector, the academic sector and from civil society (Teerawattananon *et al.* 2003; Nwokike *et al. 2013)*. The Health Promotion Foundation Act encourages the participation from all sectors in finding innovative solutions to tackle national health challenges (MoPH 2012). Results from the

interviews suggest that the MoPH meets with both academia and industry associations on a regular basis to discuss policy revisions. The TFDA conducts regular seminars and workshops with both public and private sector stakeholders. The TFDA also actively cooperates with university laboratories for post-marketing control activities. The Chulalongkorn University Faculty of Pharmaceutical Sciences Quality Control Laboratory and the Mahidol University Faculty of Pharmacy serve as regional expertise centres in the quality control of medicines and in GMP, and form part of the Asian Network of Excellence in Quality Assurance of Medicines in Thailand (Lee *et al.* 2015). Chulalongkorn supports neighbouring countries in training their laboratory staff to test the quality of essential medicines. Non-governmental (NGOs) and international organizations (IOs) also play an important role in this policy space. Some IOs, such as Management Sciences for Health (MSH) or USP, work with Chulalongkorn to conduct surveys on the quality of medicines. Phrared, a Thai NGO, is involved in raising awareness about the problems of poor-quality medicines, and in sharing information about such threats, thereby encouraging the rational use of drugs. IOs such as INTERPOL or the United Nations Office for Drugs and Crime (UNODC) have also played a role in building capacity and expertise among customs and police officials to enforce existing laws against poor-quality medicines. The UNODC supports the Thai customs in their efforts to prevent smuggling of illegal foods, including of falsified or unregistered medicines through training programs, such as those planned under the Container Control Program. Finally, INTERPOL has worked actively with Thailand since 2008 through the STORM operations I- IV, leading to the yearly arrest of drug manufacturers and sellers involved in the circulation of poor-quality medicines.

8.2.4.4   Strengthening pre-marketing and pharmacovigilance functions

Despite an elaborate institutionalization of cooperation across sector and institutions to support the process of pharmaceutical regulation and the revision of rules and regulations, the existence of the policy subsystem has not favoured the finalization of the New Drug Act to this day. A more tangible priority in efforts to strengthen the pharmaceutical regulatory system in Thailand, remains the enforcement of pre-marketing guidelines and PV activities. Regarding pre-marketing activities, Thailand accessed the Pharmaceutical Inspection Co-operation Scheme (PIC/S GMP) in August 2016, an international initiative to facilitate cooperation between competent authorities for issuing manufacturing licenses PIC/S GMP, and encourage the harmonizing of inspection procedures to improve mutual confidence in GMP guidelines across countries and facilitate exports in the region. This is a crucial step towards regulatory convergence in the region on pre-marketing regulations. Furthermore, the

industry, including GPO, cooperates with the MoPH in the development of regulation against the illegal advertising of medicines – with the aim of discouraging the irrational use of medicines or online purchasing of medicines through unlicensed e-pharmacies.

Efforts to strengthen pharmacovigilance (PV) activities include improving laboratory testing capabilities, and strengthening ADR monitoring. As pointed out in a report by USAID, Thailand regularly publishes information about drug safety in the form of bulletins. Reporting rates have been high with approximately 57,573 reports in 2011 (Nwokike *et al.* 2013). Results also suggests a gradual increase in the rate of prosecution and revocation of licenses for ADR cases. A Surveillance and Complaint Centre within the National Centre for Pharmacovigilance (NHPCV) (since 1983) was set up in 2009 to monitor complaints or reports of ADR. The NHPCV oversees information dissemination and releases alerts, information about product recalls, and annual reports on adverse drug reactions. The laboratory performs confirmatory tests on AML samples coming in from the region, in collaboration with United States Pharmacopeia (USP) in Thailand. Additionally, The New Drug Act plans to implement a product liability mechanism, whereby consumers will be able to sue drug manufacturers should the product not satisfy its intended purpose or if serious harm results from its use.

8.3   Perceptions of the problem of poor-quality medicines

In this section, I present the findings from 17 stakeholder interviews conducted in 2015 in Bangkok with representatives from the government, law enforcement organization, non-governmental organizations, academia, from international organizations, as well from the pharmaceutical industry. These findings are summarized in Table 18 on page 2001. The process of data collection in Thailand was time-consuming as there were various bureaucratic hurdles, both in terms of obtaining ethical clearance and formally requesting interviews with government institutions. Although lengthy, the procedure was well organized and steered by staff members at the National Research Council of Thailand. Despite the sensitivity of the topic, the response rates to my invitations for interviews was high. The backing of the Malaria Consortium in Thailand, as well as of the National Research Council of Thailand, was helpful in this regard. After being granted approval from senior members of the TFDA, two pharmacists working within the TFDA accepted to meet after receiving the topic guide. Responses to my set questions were pre-approved by senior members of staff. I was subsequently able to interview representatives from the BVBD and from the DMS within the MoPH in Nonthaburi. Unfortunately, I was not able to visit PPHOs across the country to obtain their insights on the circulation of poor-quality medicines in the region.

Frame	Observations
Medical	Government respondents argue that due to the lower malaria burden, poor-quality AMLs are no longer an issue but the problem might still affect other categories of medicines as well as food supplements.
Health Systems	Both categories of respondents explain that there remain gaps in the distribution of medicines, especially in remote areas and among MMPs, despite the migrant insurance scheme.
Regulatory	Government respondents highlight the strength of the regulatory framework while non-government respondents point to loohopes, including weak post-marketing surveillance efforts and the patchy enforcement of rules and regulations in border areas, as well as inappropriate penalties for medicine falsification.
Security	Government respondents frame the problem of poor-quality medicines as a threat to Thailand linked to the the MMPs, the circulation of people and goods along porous borders and weak cooperation with neighbours with weaker regulatory capacity.
Economic	Both categories of respondents agree that the strength of the domestic pharmaceutical industry and the health infrastructure development in Thailand, promotes access to quality health products. Trade liberalisation and disparities in economic development in the GMS, however, contribute to the influx of illegal goods into Thailand from neighbouring countries.
Political	Few respondents alluded to themes under this frame, but some note that the political sensitivity around the problem of poor-quality medicines hampers cross-sectoral and cross-border cooperation to reduce the circulation of falsified and substandard medicine.

Table 18 Summary of frames detailing stakeholder perception of factors contributing to the circulation of poor-quality medicines in Thailand

8.3.1   Medical Frame

8.3.1.1   Health priorities

The main term used to qualify poor-quality medicines among the respondents in Thailand was 'fake' – a term which encompassed discussions on both 'counterfeit' and 'substandard' medicines. Although there might be a noted discrepancy between the original Thai version of the definition and its English translation, my analysis of the available translated documents suggests that this use of terminology is consistent with the choice of terms in the Drug Acts. Government-level respondents regularly highlighted the importance of safety and efficacy of medicines to meet the needs of Thai patients, while placing less emphasis on the crime of drug falsification. This is consistent with the way that the problem of poor-quality medicines is presented in the Drug Acts. The general opinion among government officials was that poor-quality AMLs specifically were no longer an issue in Thailand. This viewpoint was supported by respondents from academia:

> We have the least number of fake antimalarial drugs. It's not that many anymore compared to other countries. (STK41NG_Academia20150605)

Some respondent argued that the reduced circulation of poor-quality AMLs is due to the reduction in malaria prevalence in Thailand and the reduced demand for AMLs in general. A respondent from the BVBD further explained that malaria is perceived as the 'disease of mobile migrant people' in border areas and is no longer a concern in central parts of Thailand. This is another reason why, it is suggested, malaria is no longer considered a national health priority.

> The priority of malaria is less and less […] it is not ranking as a high priority
> since a long time ago because, in the past 10 years we got 150,000 cases
> (annually) and now we have 32/33,000 cases per year.
> (STK40G_NMCP20150603)

Most respondents, including representatives from the industry, agreed that the threat of poor-quality medicines is still relevant for other essential medicines categories; such as antibiotics or treatments for non-communicable diseases (NCDs). The medicines targeted for falsification in Thailand today, they added, tend to be more widely used expensive medicines to treat NCDs, as NCDs represent the real health burden of the Thai population. One industry respondent mentioned a lack of awareness among policy makers, law enforcement officials as well as the public, on the threat of poor-quality medicines. This lack of awareness echoes the notable

emphasis at the policy level on other more tangible activities, such as PV activities and ADR reporting, and on the enforcement side – on clearer targets against the circulation of narcotics.

8.3.1.2   Traditional Medicine

Government-level respondents also alluded to traditional medicinal practices and patient preferences in response to questions about poor-quality medicines. Some explained that western or 'modern' drugs (as they are referred to in the Drug Acts) are perceived among Thai people as being ill-adapted to the 'Asian body'. One law enforcement official suggested just that:

> Sometimes in Asia if you use for Asia body, you cannot use the full dose. (STK43G_LEA20150605)

It is argued that Thai citizens tend towards traditional medicines and food supplements to self-medicate. Respondents, including representatives from the government, law enforcement and from academia, reported that the main threat to the health of Thai citizens are not poor-quality essential medicines, but rather, contaminated traditional medicines and food supplements that are illegally spiked with pharmaceutical components or with steroids. Steroid contamination is the second priority of the Royal Thai Police unit dealing with smuggled poor-quality medicines.

> The problem in Thailand is not about fake drugs actually but the food supplements that are mixed with the drugs. (STK43G_LEA20150605)

A respondent from Academia confirmed that contaminated supplements are dangerous and can be illegally purchased through online pharmacies.

> I think one thing that I found really problematic it's not only poor-quality drugs, it's also the intentionally contaminated dietary supplements with dangerous drugs, and we find that on the internet. (STK51NG_Academia20150916)

The threat posed by e-pharmacies was a pervasive topic throughout all interviews conducted in Bangkok with both government and non-government respondents, who suggest that the high demand for traditional medicines and food supplements in Thailand has created an opportunity for dangerous, poor-quality products to be sold through pharmacies.

…[O]nline purchasing is a problem, it's very difficult to assess the extent of it. (STK48NG_LNGO20150907)

An additional factor said to promote the sale of such medicines online, is the illegal and unregulated advertising through social media of medicines and traditional supplements which make unsubstantiated claims. Under this theme, respondents mentioned the socio-cultural habit of self-medicating. As this frame suggests, respondents seemed to have a different perception of medicine quality, with a greater emphasis on poor-quality lifestyle drugs and the contamination of legitimate products, including food supplements, rather than on medicine falsification.

8.3.2 Health Systems Frame

8.3.2.1 Access to medicines

Under this first theme, both categories of respondents concurred that the challenge of poor-quality medicines is intrinsically linked to issues of access to medicines and the general health system. A respondent form a Thai NGO explained that despite efforts to improve health coverage across Thailand, some remote hill tribe communities in the northern part of the country still have limited access to hospitals and to medicines:

> People in the border areas, don't have access to many health facilities. Access to any health services is difficult. In Thailand, we have malaria clinics scattered near the border but it's not as close to each other as here in Bangkok between hospitals. It's quite a distance. (STK48NG_LNGO20150907)

This gap in access to medicines might create a demand for medicines from alternative sources. It is perceived that MMPs working in the forests of Thailand's border provinces who may not have access to the free malaria clinics (due to their geographical location and despite the migrant insurance scheme), are tempted to purchase their medicines from itinerant drug vendors as illustrated in the quote below:

> People with a backpack, with certain kinds of drugs (illegal) travel around seeing those guys in the forest and provide care and sell drugs. (STK40G_NMCP20150603)

> Substandard, fake drugs for antimalarials is not really a problem, but it is a problem for those who stay in the forest and have difficulty of accessing drugs. (STK40G_NMCP20150603)

Government respondents explained that drugs that are both expensive but also hard to obtain often end up being sold on the black market – as is the case for abortion pills. The latter are often purchased from the internet by teenagers, as they have no other legitimate means of getting them without being stigmatized. Providing essential medicines for free is perceived as key to improving access to *quality* medicines and helping to reduce the circulation of poor-quality medicines:

> One of the methods is making sure there is access to the quality ones everywhere so that nobody has to go buy it from dubious sources. (STK49G_NRA20150911)

This corresponds with the emphasis on improving universal health coverage in Phase II of the policy process. Regardless, not all MMPs register to be treated in the Thai public health system and despite initiatives to achieve Universal Health Coverage, some MMPs continue to work and live in Thailand without declaring their presence and are unable to access malaria treatment for free (USAID 2014). As a result, some may seek treatment for malaria through alternative sources, thus fuelling a black market of essential medicines of dubious quality.

8.3.2.2   Distribution of essential medicines

Both government and non-government respondents also linked the problem of poor-quality medicine to the distribution of medicines. Some respondents highlighted the strength of the Thai health care system in this regard. Respondents from academia, for example, explained that current regulations do not allow pharmacies to sell AMLs, therefore implying that all AMLs found in pharmacies are potentially of illegal source and could be of poor-quality.

> There are regulations saying that all AMLs have to be used in healthcare facilities only. It's not legally available in the drug stores. That is one good initiative from Thailand, to restrict this drug to health care facilities but not to pharmacies. (STK42NG_Academia20150605)

The BVBD added that Village Health Workers (VHWs) help secure a continuous supply of treatments to patients in the more remote areas of Thailand, ensuring that no one is required to purchase treatments from unlicensed sources.

Despite such measures, however, other respondents explained that distribution guidelines are not always enforced adequately. For example, 'special-controlled drugs' or prescription-only medicines are often dispensed without prescription.

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> In theory, you get prescription but in reality, the prescription system in Thailand doesn't work so much. (STK50G_NRA20150911)

Reports confirmed that prescription-only drugs, including antibiotics, are still available over-the-counter in Thailand, despite efforts to enforce dispensing guidelines and improve the rational use of medicines (Lee *et al.* 2015; Pongpisut *et al.* 2015). Medicines are still being distributed in the form of '*ya-chuut*' or 'cocktails of drugs'. As discussed in the previous chapters, this could be evidence of poor distribution practice and may contribute to the circulation of poor-quality medicines, as it is difficult to verify the packaging and content. While the New Drug Act proposes stricter rules for the dispensing of medicines, stipulating that issuing 'cocktails of medicines' in plastic bags will no longer be permitted, this Act has not yet been promulgated and undermined efforts to improve Good Distribution Practices.

Respondents from the BVBD and academia also discussed the problem of substandard and degraded AMLs fuelled by poor distribution and storage practices, including the 'improper handling of drugs in malaria posts' with suboptimal temperature or humidity levels.

> The thing we should do is go out, look at how they handle drugs, stock drugs, look at the temperature they use, etc. Promote the better management of drug stocks. (STK40G_NMCP20150603)

Most respondents therefore admitted that there is still room for improvement in Thailand with regards to the distribution of medicines. Industry representatives reported that the problem of poor-quality medicines lies predominantly in the illegitimate supply chain and distribution of medicines through illegal e-pharmacies and the black market. As a respondent from Chulalongkorn University pointed out, the government is currently working to improve trust in public health facilities and to dissuade patients from purchasing medicines from dubious sources, such as online pharmacies. This echoes the emphasis on strengthening pharmacovigilance activities in Phase IV of the policy process.

8.3.3   Regulatory Frame

8.3.3.1   Rules and Regulations

Government-level respondents argued that the Thai regulatory framework for pharmaceuticals is well developed and that the prevalence of poor-quality medicines is relatively low compared to neighbouring countries. Respondents from the Ministry of Health referred to the strength of Thailand's pre-marketing rules and regulations for AMLs and explained that some aspects of

Thailand's vertical malaria programme have worked efficiently to prevent the circulation of poor-quality AMLs.

> …[E]very type of [AML] drug from procurement to distribution belongs here to the BVBD. It is not allowed to the free market - then it is easy to control the quality of the product. (STK40G_NMCP20150603)

> We don't have problems with antimalarials…because the BVBD does appropriate procurement for antimalarials. [The BVBD] distribute all over the country. [The BVBD] prove the quality before we distribute so we can reduce the problem of the [poor-] quality [AMLs] reaching the system. (STK44G_MoH20150609)

Most respondents, both at the government level and among academia, added that Thailand has a strong medicine quality testing facility, which neighbouring countries also benefit from by sending samples through for quality control. Respondents from the TFDA and Department of Medical Science pointed out that some countries even take example on Thai GMP standards to update their own regulatory frameworks. Respondents from the TFDA emphasised that if neighbouring countries were to follow the Thai pre-marketing standards, it would help to reduce the problem of poor-quality medicines in the region altogether.

Despite the strengths of the framework highlighted above, some non-government respondents pointed out that there remain loopholes in the system that could be exploited by pharmaceutical criminals. Some argued that the current penalties for the production, distribution and sale of poor-quality medicines are not representative of the severity of the crime. Most acknowledged the need for stronger penalties – currently being discussed in the New Drug Act. Industry representatives' concern towards the current penalty revisions, as seen previously, suggests that fears of more inadequate penalties have contributed to the stalling of New Drug Act approval process. It is also important to note here that there are no specific clauses on the illegal sale of medicine in online pharmacies (Homhuan 2013). Other respondents reported that the main weakness of the drug regulatory system relates to Market Authorization (MA) guidelines currently allowing the lifetime registration of pharmaceuticals. MA certificates for registered medicines do not have an expiration date – meaning that no renewal procedure is required. There is therefore no systematic mechanism to review MAs for medicines registered over 10 years ago, that may today be ill-suited to the current health needs of the country. The revised Drug Act (2003) proposes to reduce the validity of the certificate of product registration to five years, however, this Act has not yet been promulgated, as previously explained.

> They have to revaluate the existing registrations because our registration is for a lifetime, so they don't revaluate [the medicine] – [it is] registered 22 years ago or more like 30 years ago. We need them to get rid of those that are poor [quality]. (STK51NG_Academia20150916)

A related challenge identified is the lack of regulatory measures taken to ban the sale and distribution of Oral Artemisinin Monotherapies (oAMTs) in Thailand. Since MAs do not expire, oAMTs are technically allowed to circulate in Thailand and there are no measures to monitor the use of such medicines by malaria patients. This poses a threat for the rational use of medicines and access to adequate treatment to eliminate malaria.

As a result, the market is crowded with medicines still registered but with minimal use. It is suggested that this makes it more difficult to discern which products may be registered, unregistered, or fake. While some respondents argued that the procurement system organized through the GPO has improved the management of what is a crowded supply chain of medicines, others argue that in practice the procurement system for essential medicines remains very complex. A professor from academia explained that the high number of wholesalers who repackage and re-label medicines not only complicates the supply chain, but also makes it difficult to track the source and the quality of the products along the way.

> …You have rule(s) on the procurement… So, it's a mixed process. It's not really centralized or decentralized, it's a mix and it is quite complex. (STK51NG_Academia20150916)

Respondents added that the logistics management system and cold supply chain system in Thailand still needs strengthening to effectively prevent the circulation of poor-quality medicines.

8.3.3.2   Weak surveillance and enforcement capacity

Most government-level respondents highlighted the strengths of Thailand's post-marketing surveillance framework alluding, for example, to the fact that TFDA inspectors work in collaboration with customs officials at ports of entry – both at the central and provincial levels. As a result of such initiatives, the DMS highlights that the percentage of poor-quality medicines has considerably reduced over the years from 10% to 5%. Nevertheless, non-government respondents and Thai academics argued that post-marketing surveillance activities in Thailand could be improved. Respondents explained that the sampling strategy of the DMS for medicine quality control is executed in an unsystematic way, implying that samples are not

randomly chosen across therapeutic categories and outlets for quality testing, but are often obtained from sources where regulators are less likely to encounter poor-quality medicines, i.e., large hospitals rather than border clinics. Such gaps in PMS are confirmed in a report which suggests that the sampling process does not effectively monitor the quality of all essential medicines including AMLs (Lee *et al*. 2015).

> One of the problems why we have so many substandard medicines is that we don't have a method to evaluate the quality of [all] the product[s]…Some antimalarials are in pharmacopoeia but a lot of them [are not], especially the new combinations. (STK41NG_Academia20150605)

As seen previously, AMLs are not part of the sampling efforts of the DMS and are tested separately by the BVBD. The BVBD works alongside USP with funding from WHO and USAID to implement ad hoc inspections on AMLs. Yet, the 2011 malaria control plan provides no indicator for measuring the percentage of poor-quality AMLs in Thailand (MoPH n.d.). Respondents also argued that AMLs should be systematically included in the annual drug-quality testing rounds, and should be collected from border provincial areas. This may not currently be the case because malaria is no longer perceived as a health priority, and as a result, respondents explained that less funding is made available for the systematic sample collection and quality control of AMLs.

Most respondents across categories also argued that the enforcement of existing rules and regulations for the management of pharmaceuticals are particularly patchy in border areas.

> We know that for suburban areas, quite far from the capital, in some regions, we can't go to them. But now, in big cities we can control. In rural areas, we cannot control 100% but we try. (STK44G_MoH20150609)

A customs official interviewed for this study added that there are different standards of enforcement from place to place between the central and peripheral areas of Thailand, suggesting that while pharmaceutical regulation is strong in Bangkok and its vicinity, laws are not always enforced as they should be in provincial border areas. According to a local NGO, this may be due to a lack of resources – both human and financial – to actively survey the situation in those areas further from the central TFDA. Respondents agreed that there is a lack of qualified pharmaceutical inspectors to enforce post-marketing activities. In principle, inspections on pharmacies and drug outlets are conducted before re-issuing licenses. In practice, however, although inspection responsibilities are delegated to PPHOs, reports suggest that there are insufficient staff members across the country to conduct inspections in

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all outlets. Yearly renewals are said to impose a burden on the TFDA for pre-marketing activities. Both factors could potentially facilitate the circulation of poor-quality medicines. It is also reported that while online pharmacies are illegal, the closure of e-pharmacies is not enforced. The threat of technology and the difficulty of regulating online commerce is perceived as a major challenge:

> There are a lot of fake drugs like that on the internet, they just change their identity and it's done. And they will always have customers. (STK40G_NMCP20150603)

A respondent from law enforcement explained that some factories licensed by the TFDA produce substandard medicines but escape inspections because police officials assume that their license is a certification of quality for all their products. This, law enforcement respondents argued, calls for a strengthening surveillance and more awareness raising among law enforcement officials as well as policy makers (STK45G_LEA20150609). They also explained that narcotics law is better understood and receives priority attention among customs officials on the ground. Another respondent added that arrests against unlicensed outlets are only performed for 'big cases' that might attract more media attention, but that enforcement is weaker for smaller outlets where the presence of poor-quality medicines may be considered less consequential (STK43G_LEA20150605).

8.3.3.3   Lack of cooperation

Finally, many respondents argue that cross-sectoral collaboration is essential for effective enforcement of existing laws and policies:

> The authority is not the main player in the problem of quality of medicines. It should include industry, academia. Everybody should collaborate to improve the quality of the medicines. (STK42NG_Academia20150605)

Most respondents explained, however, that cross-sectoral cooperation is not always optimal. One industry representative, for example, explained that there is a general reluctance to share information about poor-quality medicines for fear of insulting the regulators and damaging their cooperation with the government. This points to a certain level of sensitivity on the topic of regulatory enforcement. Interestingly, no respondent mentioned the 2009 Memorandum of Understanding cited in the literature. It seems that while most respondents acknowledge the need for cooperation; the institutionalization of such cooperation remains weak. Respondents also highlighted the need for more communication between the TFDA and the BVBD in

running the malaria program, and ensuring a continuous supply of good quality AMLs to achieve malaria elimination by 2024. Furthermore, a representative from a law enforcement agency commented on the status of cooperation between customs and police over poor-quality medicines:

> Cooperation is not that efficient though as both parties are too busy and can't concentrate on all issues. (STK45G_LEA20150609)

On this point, a respondent from the Royal Thai Police added that to close an online pharmacy website, the Consumer Protection Unit must seek the help of the Information Communication Technology unit. In practice, the process is complicated and rarely applied, as many enforcement officials are afraid to infringe on the business of those website owners who may not be selling only pharmaceuticals.

> How to close the website; I need to arrest the website first, write down a document to the other police division (the ICT police). They will send the letter to the court to tell them about the problem. The court will decide to close the website or not. It takes a lot of time. Only one month or one week they sell a lot of products via the internet, maybe a million pieces. (STK43G_LEA20150605)

Respondents agreed on a lack of clarity and certainty on enforcement procedures against illegal online pharmacies. This process, they argued, needs to be optimized together with the MoPH. It was also reported that Police departments require more authority to share information to the public on which websites have been found to sell poor-quality medicines and should be avoided.

Respondents previously pointed out the need for more cross-border cooperation, however, government respondents and law enforcement officials mentioned unsystematic cooperation with neighbouring countries on the matter of pharmaceutical regulation. Despite attempts to cooperate with NRAs beyond Thailand's borders, these efforts rarely lead to arrests. Respondents also referred to the inefficiency of harmonization and cooperation initiatives through ASEAN (STK45G_LEA20150609). One anonymous respondent explained that ASEAN's unanimity decision-making principle means that few decisions are taken that benefit regional cooperation. Another respondent added that police officials in neighbouring countries are not aware of how to get in touch with their Thai counterparts to exchange information on the potential circulation of poor-quality medicines (STK43G_LEA20150605). Additionally, INTERPOL meetings, while useful, are rarely attended by the same members of staff in each unit, which does not facilitate fluid contact and cooperation across borders.

8.3.4 Security Frame

8.3.4.1 Dynamics of migration

Under the security frame, government-level respondents referred to the cross-border movement of MMPs and the threat of illegal smuggling as factors potentially contributing to the circulation of poor-quality medicines in Thailand. Respondents perceived MMPs seeking health care in Thailand as posing a threat to the system. Because of the social security schemes in place for MMPs, this influx of MMPs seeking jobs in Thailand's border provinces places a high burden on Thai hospital and strains the health care system, leading to budgetary cuts which it is argued can affect access to free essential medicines for Thai citizens. The overuse of Thai health facilities, they argued, might make it more difficult to overcome stock-outs of medicines. Yet, despite efforts from the Thai government to facilitate MMPs' access to health services and despite the signature of an MoU between Thailand, Cambodia, Laos and Myanmar on the issuance of a health insurance cards for migrants registered to work in Thailand, some are still unregistered and without proper access to health (STK55NG_INGO20150910). Some of those are involved in illegal logging activities, for example. Despite efforts to provide standard health kits for access to basic health commodities for unregistered forest-goers such as illegal loggers, their access to quality healthcare is compromised (STK54NG_INGO20150910). It is reported that unregistered MMPs drive the demand for poor-quality medicines by purchasing commodities from itinerant sellers at the border. Other respondents added that certain migrant communities prefer to bring their own medicines they are familiar with, thereby favouring the cross-border trafficking of medicines that may not be registered in Thailand.

> They [poor-quality medicines] are manufactured somewhere else and they come
> in through migrants to the border areas. (STK42NG_Academia20150605)

Other respondents explained that migrants may be afraid of using Thai healthcare services if unregistered, for fear of being sent back home. Registered migrants may also not be aware of their entitlement to free or subsidized healthcare in Thailand. These factors may drive migrants to self-medicate and purchase medicines such as AMLs from unlicensed outlets, possibly fuelling the trade in poor-quality medicine. The other challenge highlighted by government respondents, is the risk of spreading artemisinin resistance through MMP movements.

> What they do is they go directly to grocery stores where they have these AMLs
> and they buy it there. They don't get a proper treatment and that's where they find
> antimalarial drug resistance. (STK41NG_Academia20150605)

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8.3.4.2   Regional threat

The second theme under this frame, addressed by both categories of respondents, was the perceived threat posed by neighbouring countries such as Myanmar, Laos, or Cambodia where poor-quality medicines is thought be more of a problem. A customs representative argued:

> …[R]aw materials [for the unlicensed production of pharmaceuticals] usually trace back to China or India. Assembly wise, they've seen it take place in Cambodia. I mean the packaging of raw materials. Now it's shifting as Cambodia has stepped up on their enforcement. Some of it shifted to Myanmar. (STK47NG_20150915)

One anonymous respondent from an IO reported that the border with Myanmar is of concern especially due to weak regulation capacity on the other side of the border, the political instability and rebel activity at the border, as well as the geography of what is a highly mountainous or with rives and few formal checkpoints. A respondent from a Thai NGO expressed scepticism at the government's capacity to control every area of Thailand's long and porous border, where there are both formal checkpoints and numerous informal entry points, such as along the Mekong River.

> The river is very easy to cross you can just take a boat and go. and sometimes you can just walk. (STK54NG_INGO20150910)

In view of the porosity of the borders and the establishment of the ASEAN Economic Community, respondents concur that cross-border cooperation between Mekong countries is necessary to address the threat of poor-quality medicines, especially at border check points.

> We need to improve cross border cooperation in view of AEC 2015 – this will represent an additional challenge due to the free flow of goods. (STK54NG_INGO20150910)

8.3.4.3   Organized Crime

The third theme brought forward by both government and non-government respondents is the regional challenge of organized crime and the smuggling of illegal products into Thailand – all phenomena that potentially contribute to the circulation of poor-quality medicines. Respondents from the industry, from an IO and from the TFDA mentioned the strong link between the trade in narcotics in the region and the trade in fake medicines. One respondent argued that both have similar distribution channels and modus operandi. Respondents added

that the low penalties incurred for the falsification of medicines has attracted narcotics criminals into the business of medicine falsification. While there is no proof of links between the two criminal networks, respondents argued that the falsification of medicines may be a more resilient option than narcotics trade, with fewer risks of prosecution.

A customs official noted that the perception of law enforcement officials hinders efforts against poor-quality medicines, as many law enforcers still consider the narcotics trade as 'a more important crime' (STK45G_LEA20150609). This, the respondent argued, may be partly due to their familiarity with the implementation process of existing regulation against the narcotics trade. Another law enforcement respondent suggests that there is a lot of sensitivity around reporting pharmaceutical organized crime run by 'big businesses' or organized criminal enterprises. This fear may also impede on efforts to address the circulation of poor-quality medicines:

> They don't want to make a problem with anybody. I mean people who have big businesses – businessmen make this and sell people around that area. (STK43G_LEA20150605)

The second main point brought forward is the high level of smuggling of different types of fake goods along the Thai border, from fake cosmetics from China, narcotics, to motorcycles or unregistered medicines.

> Viagra (unregistered) is a big issue here. Most of those come from Pakistan or India and are smuggled in. (STK56G_20150914)

Respondents argued that falsified medicines are brought into Thailand in the same way that narcotics, or fake DVDs may be smuggled in. A respondent from Chulalongkorn University added that addictive substances are smuggled into Thailand to be added to traditional medicines – which is one other example of how the narcotics and the poor-quality medicines trade are intertwined (STK51NG_Academia20150916). The intensity of this illegal trade, respondents argued, is too much for law enforcement officials to deal with. A respondent from a Thai NGO added that despite cooperation efforts and the help of the World Customs Organisation, the routes are hard to trace back using the information on the packaging, seeing as the labels can be just as fake as the contents of the medicine (STK48NG_LNGO20150907). Another respondent explains that despite cooperation efforts through the Joint Mekong River Patrol against smuggling of illegal products in the region, cross-border cooperation efforts are once again mainly focused on the narcotics trade (STK46NG_IGO20150610). Finally, a customs official added that this illegal trade is an essential part of the Golden Triangle's

economy and that cracking down severely would affect the whole economic cycle of the region (STK45G_LEA20150609). This links to the next Frame on the economic determinants of the trade in poor-quality medicines.

8.3.5   Economic Frame

8.3.5.1   Industry

On numerous occasions, and across respondent categories, the threat of poor-quality medicines was dismissed and discussions re-directed to the strength of the domestic pharmaceutical industry, presented as one reason why poor-quality medicines are no longer a major threat in Thailand. Respondents explained that the GPO produces a wide array of medicines across therapeutic categories at affordable prices and the fact that most medicines can be supplied through the domestic pharmaceutical industry, they added, means that less imports are required thereby reducing the risk of poor-quality medicines entering Thailand. Others argued that pharmaceutical companies have an important role in efforts against fake medicines as they offer trainings to customs officials on quality assessment for batches of their products. Members of the GPO framed the ASEAN Economic Community 2015 efforts towards the harmonization of pharmaceutical registration procedures as an opportunity for Thailand to export its medicines, first and foremost, besides offering prospects for securing medicine quality across the region. In their answers, other respondents re-iterated the importance of GMP and the recent application of Thailand to PICS as an incentive for domestic drug manufacturers to improve their facilities. Both government and non-government respondents placed a strong emphasis on IP protection in Thailand, thus discussing the threat of poor-quality medicines as a trademark infringement and a peril to the industry. In their accounts, law enforcement officials also regularly confounded the problem of fake medicines with that of 'counterfeiting'. On many occasions, efforts to improve access to quality medicines were regularly equated to the development of the pharmaceutical industry and the preservation of business interests.

Other respondents explained that despite regulations against the inappropriate advertising of pharmaceutical products, it is common to find adverts for unregistered, poor-quality supplements, or medicines of dubious origin, especially in social media. They explained that the main target for this industry are young people, who are sensitive to advertising through Facebook, for slimming pills or other lifestyle medicines. These marketing tricks, they argue, drive the trade in poor-quality medicines of all categories:

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> Young people they don't understand they don't see the news; they don't read the newspaper. But they use telephone or the internet [technology and health seeking behaviour] they Google 'cheap fat burning supplement' 'cheap supplement for white skin'. They see many products. (STK43G_LEA20150605)

According to respondents from GPO, TFDA and academia, enforcing regulation against these advertising techniques (as was done against the promotion of tobacco products) is one of the current priorities of the MoPH. Another challenge noted by respondents, was the lack of cooperation in terms of information sharing by pharmaceutical companies, arguing that most companies 'don't want to cause panic in a particular market', and would chose to deal with uncovered stocks of poor-quality medicines quietly rather than alert the authorities (STK47NG_20150915). This alludes to fears of interfering with business, the same fears that are said to impact enforcement efforts.

8.3.5.2   Development and infrastructure

Respondents from both categories also referred to infrastructure development as both a support for efforts against poor-quality medicines and as further evidence of the development gaps between neighbour countries, that lead to variations in in access to quality services and health commodities. Firstly, respondents discussed the positive aspects of Thailand's infrastructure development. Better health facilities and road networks across the country have dramatically improved access to health services and to medicines. Malaria clinics and posts in the more remote areas of the country are a testimony to this. A respondent from the BVBD added that in Thailand, most malaria endemic villages do have access to electricity and are not as remote or secluded as they may be in other less developed malaria endemic nations (STK40G_NMCP20150603). It is economic growth that drove social development in Thailand and engendered a demand for higher quality health services, leading to the introduction of the social security scheme in the 1990s, as explained in the literature (Teerawattananon *et al.* 2003). On the other hand, respondents pointed out that in neighbouring countries where there may be fewer resources for infrastructure development and a lack of health facilities, access to health and to medicines suffers. This is one aspect, respondents agreed, that may continue to drive the region's trade in poor-quality medicines and why such products might find their way into Thailand's border provinces. While transportation routes, such as the East-West Economic Corridor, have facilitated trade, economic and social development across the Mekong region, weak regulation and poor customs control, especially in the lower-income countries, creates an opportunity for the smuggling of illegal goods of all kinds, including poor-quality medicines. One respondent explained that there are concerns with the trade routes

that go through Myanmar, for example. This links back to the security frame, as detailed in section 8.3.4.

8.3.5.3   Trade liberalization

In their accounts, non-government respondents referred to the income disparity between economics of a region in transition, as an obstacle to securing the supply chain of good-quality medicines. Respondents referred to regional investments as exacerbating the economic gap between Mekong countries, increasing disparities and fuelling the illegal movement of goods and people. In fact, globalization and the cross-border movement of goods and people, is acknowledged in the 11th National Health Development Plan 2012-2016 as one of the main health challenges for Thailand. A respondent from Chulalongkorn University suggested that too much emphasis on economic development and trade in the region has overlooked social priorities for improving the health and wellbeing of Mekong citizens (STK51NG_Academia20150916). The respondent added that poor communities suffer from inequitable regional investments, and urged that growth be more inclusive to support access to medicines for all. Respondents from IOs stated that this region in transition offers many opportunities for money laundering in the form of hotels or shopping centres, as witnessed in Myanmar or Laos. They added that the health landscape of the Mekong is changing with wealthier countries in the region building hospitals across their borders for their own citizen. This, they argued, offers opportunities for a parallel trade of medicines that NRAs might be ill-prepared for. Respondents also argued that trade liberalization in the wider region of Southeast Asia and Free Trade Zone has increased opportunities for smuggling, due to poor regulation of cross border movement. While Free Trade Zones should be free of tariffs they are too often free of customs control altogether, facilitating the movement of illicit goods including, potentially, of poor-quality medicines.

8.3.6   Political Frame

Few of the themes that emerged from respondents' accounts in Thailand fell under the Political Frame. One main observation can be made from the narratives, however, that alludes to the political sensitivity in Thailand and in the region around the problem of poor-quality medicines. An industry representative noted that at a luncheon held on access to safe medicines with ASEAN countries, there was reluctance to join, on the pretence that poor-quality medicines were not considered an issue for Thailand due to its development nation status (STK47NG_20150915). A respondent from a law enforcement agency explained that for fear of upsetting working relations with Thailand, policy officials from abroad are reluctant to share

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information about fake medicines at border areas, for fear of uncovering sensitive information that would place blame on one country or another.

> I've tried to tell the police abroad that if they have information about fake medicines from Lao or Myanmar or Cambodian people, let me know and I will check myself in Bangkok, I will follow the information. They don't want to make a problem with anybody [sensitivity]. (STK43G_LEA20150605)

Respondents rejected the possibility of poor-quality AMLs still being in circulation in Thailand, emphasizing the fact that the demand for AMLs has considerably reduced, that malaria is a low public health priority and is now mainly a disease of the MMPs and of neighbouring countries. There was notable sensitivity when addressing the problem of access to medicines among MMPs and the possibility of poor-quality medicines still circulating in border areas. When asked to develop on this point, one respondent from a local non-government organisation asked me to turn off the microphone. In fact, respondents from Academia mentioned that the problem of 'fake medicines' is addressed sporadically only when the news picks up on large case:

> When there is news on fake medicines, it brings attention to this issue for a while and people say they want to combat counterfeit drugs but I don't think the issue is that big in Thailand that it secures an established process, a regular process. (STK41NG_Academia20150605)

A respondent from law enforcement added that the problem of contaminated or poor-quality cosmetics and food supplements, received more political attention; impeding law enforcement officials' ability to invest time and resources into the problem of poor-quality pharmaceuticals:

> Activities focus on cosmetics and supplements. Cooperation [between customs and policy] is not that efficient though as both parties are too busy and can't concentrate on all issues. (STK43G_LEA20150605)

8.4 Frames and the policy process

The problem of poor-quality AMLs is not perceived as an issue of the highest political priority in Thailand, mainly because malaria no longer accounts for much of the disease burden in the country. Results suggest a different understanding of the problem of medicine quality among regulators, with a focus on the issue of substandard pharmaceuticals including contaminated traditional medicine and food supplements. The results also suggest that Thailand is faced with a new kind of challenge; one that may be equated to a more developed economy where the disease burden is predominantly related to NCDs, where the demand for lifestyle medicines is

high and where many consumers have access to the internet and prefer purchasing their medicines through illegal online pharmacies. The online sale of medicines in a growing health sector of an upper-middle income nation with widespread access to the internet, is indeed recognized as an important challenge to accessing good quality medicines. This observation seems to echo the government's emphasis lately on tightening regulations against illegal advertising of medicines, and a focus on PV activities to monitor ADR, as described in Phase IV of the policy development process.

The regulatory challenges of tomorrow in Thailand, triggered by economic development and the rise of technology and e-purchasing, appear to be different to those faced by neighbouring countries. Most respondents agree, however, that while poor-quality AMLs may no longer be the main priority in Thailand, new challenges require the regulatory system to adapt; which might explain the urge to agree on the New Drug Act revision. While the reasons for the delay in promulgating the New Drug Act are unknown, recent political turmoil in Thailand could have slowed the revision process and submission to parliament, as might the level of bureaucracy incurred in large drug regulatory agencies such as the TFDA. Regardless, the fact that the promulgation process for the New Drug Act may have triggered regulators to focus first and foremost on PV activities and ADR monitoring; an area where activities are less politically sensitive and in which regulators can achieve tangible results.

The results also suggest that the region-wide threat of drug resistant malaria could have contributed to the government's effort to improve UHC. It was suggested that concerns that poor access to quality AMLs in border areas might exacerbate the risk of chloroquine and subsequently of artemisinin resistance spreading in Thailand, may have prompted efforts to include migrant workers in a compulsory health insurance scheme. Additionally, because of a rapidly growing public health sector, a high number of medical tourists from neighbouring countries now seek treatment in Thailand's hospitals. This, respondents suggested, has placed a considerable burden on the health system and could also have formed part of the government's motivation to improve UHC for its own citizens and residents as well. The pressure exerted on Thailand to guarantee the health of its residents and of MMPs, as a middle-income economy, may also have motivated these efforts. This testifies to a strong policy response to improve access to quality-assured medicines.

Despite a reportedly comprehensive pharmaceutical regulatory framework (Teerawattananon *et al.* 2003) and despite the government's considerable efforts to improve access to quality-assured medicines, results also suggest room for improvement in terms of both pre- and post-

marketing regulatory activities. While government-level respondents emphasized the fact that the Thai regulatory framework is an example from which neighbouring countries can gain expertise (for example, Thailand positions itself as a reference laboratory for quality testing pharmaceuticals), most non-government respondents suggest that more could be done to optimize the enforcement of existing rules and regulations. It appears that despite the existence of a large policy subsystem to debate health regulation and reforms among stakeholders from various sectors, cooperation between the concerned parties when it comes to the implementation and enforcement of rules and regulations is more challenging. Respondents explained that the decentralization of PMS activities to peripheral areas has not been implemented optimally. Additionally, respondents suggested that law enforcement officials have a better understanding and training for monitoring the illegal circulation of narcotics rather than medicines, as the narcotics trade remains a priority national health and security concern in Thailand.

Another particularity of the Thailand context is the importance of the pharmaceutical industry and of trade interests. The economic frame seems to be a common thread from Phase I to Phase IV of the policy development process. The prevalence of industry has been suggested as one of the potential reasons why the process to finalize the New Drug Act (2003) has stalled, in view of disagreements with industry representatives. However, greater trade opportunities between ASEAN countries also create opportunities for the circulation of illegal goods through established trade routes. This makes effective border control more challenging, and heightens the risks of poor-quality medicines circulating in Thailand. Respondents contended that the impact of economic development on countries' capacity to regulate is undeniable and that Thailand has comparatively more capacity to regulate and manage the quality of medicines in its supply chain. Thailand's current focus on PV and ADR activities is commensurate with policy actors' concerns for resolving the problem of contaminated supplements, improving ADR report and keeping a low statistical prevalence of poor-quality medicine.

Chapter 9   Discussion

The global issue of poor-quality medicines is a multi-faceted and complex challenge. Results show that how the challenge of poor quality antimalarials (AMLs) is framed, influences the way in which policy actors in Cambodia, Laos and Thailand formulate policy responses and implement rules and regulations to improve access to quality medicines. The introduction to this thesis laid out four main goals for this research: 1) to examine the policy developments against poor-quality AMLs in these countries; 2) to explore how the problem of poor-quality medicines is framed by stakeholders in these same countries; 3) to compare the similarities and differences in how this issue is framed; and 4) to reflect on the implications of research findings for future policy developments and cross-border coordination against poor-quality medicines in Southeast Asia. In this chapter, I first compare how the policy issue of poor-quality AMLs is framed across national settings and reflect on the implications of variations in the problem definition for pathways of policy response. Because of the importance of the socio-economic and political context, the politically charged nature of the issue of poor-quality medicines and the varying governance structures and differences in regulatory capacity between the countries studied, I reflect on the benefits of a tailored approach to strengthening regulatory systems. This can still be facilitated by a regional governance framework to foster regional cooperation and promote policy coherence.

Examining varying interpretations of the problem among policy actors in three different national settings, and how these interpretations relate to the policy development against poor-quality AMLs, led to some interesting empirical findings. Three main findings emerge from the comparative analysis of the frames and policy processes in Cambodia, Laos and Thailand: 1) Despite variations in the terminology used to define poor-quality medicines, there are three dominant and common frames (the security, health systems and regulatory frames) among policy actors that presuppose a shared understanding of the threat of falsified and substandard medicines across the three national settings, based predominantly on the security paradigm. This provides some insights as to what narrative might trigger or sustain political will towards the ATM goal. 2) These frames are articulated differently in each country leading to different policy outcomes, shaped by policy actor mobilisation and specific contextual factors. 3) Results suggest that there is room for addressing variations in pathways of policy response by pushing the regional health security agenda to encourage broader health systems strengthening and, where relevant, to harness regional cooperation.

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9.1 Problem definition: Framing poor-quality medicines

One main observation from the results of this study is that poor-quality medicines are defined differently across national settings in official policy and legal documents. These variations in definition influence how frames resonate among groups of actors and policy environments. The inconsistency of official definitions across national settings, however, means there is no common legal or medical understanding of the challenge posed by poor-quality medicines. This reduces opportunities for cross-border coordination of policy responses (Attaran, Barry, et al. 2012). The terminology used to define poor-quality medicines in official legal and policy documents is inconsistent across the three countries (as summarised in Table 19 page 223). In the official English translations of policy documents, the terms used interchangeably are 'counterfeit', 'fake', 'substandard', 'non-standard', and 'deteriorated' medicines[52]. Most policy and legal documents, however, refer to 'counterfeit' medicines or offer definitions of poor-quality medicines that centre around trademark infringement (such as those in Thailand or Cambodia). In Thailand, the term used most frequently is 'fake' rather than 'counterfeit', but the matching definition centres on trademark infringement. This confounds the public health priority of consumer and patient protection with intellectual property protection. There is rarely a distinction made in official definitions between substandard and falsified (or counterfeit) medicines. Laws for the management of pharmaceuticals in Laos, for example, refer to counterfeit, substandard and deteriorated medicines, as well as unqualified, banned or prohibited medicines interchangeably. Additionally, the notion of 'intent' which is an essential legal differentiation between 'falsified' from 'substandard' medicines (Attaran *et al.* 2011), is rarely part of official definitions of poor-quality medicines (except for the Laos' Amended Law on Drugs (2011, article 3.3)). This amalgam of terms complicates the development of adequate national policy responses to each category of poor-quality medicines. Official definitions of poor quality medicines lack clarity and consistency. In most cases, these definitions fail to address the complexity of the issue of poor-quality medicines as multi-faceted challenge, requiring different policy responses for substandard and falsified medicines.

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[52] These observations are based on English translations of official documents which I did not review in their original languages. The original terminology in Thai, Lao or Khmer may therefore differ slightly from those put forth in English translations. This represents a limitation to this study, as will be discussed later in this chapter.

Country	Document	Definition
Cambodia	Amendement of Law on Management of Pharmaceuticals (2007) Article 2.2	'A counterfeit pharmaceutical is a medication which may contain inactive ingredients or inappropriate quantities of active ingredients, or may not contain enough active ingredients as mentioned on the label, or has the packaging, design, identification similar to or the same as the original products or may be produced or packaged without licensing from the Ministry of Health.'
Laos	Amended Law on Drugs and Medical Products 07/NA (2011) Articles 3.3 and 3.4	(Article 3.3) 'Counterfeit drugs and medical products refer to any modern drugs, traditional medicines, medicinal natural resources, cosmetics, health supplement, medical devices, controlled chemicals and dangerous chemicals which are intentionally falsified or imitated or copied from the products which are produced, distributed and legally registered.' (Article 3.4) A 'Sub-standard drug refers to a modern drug or traditional medicine, the composition of which is not consistent with its registered formulae.'
Thailand	Drug Act 1967 (Section 74)	A Fake Drug is a drug that 'falsely shows it is in accordance with a formula which has been registered' or one 'with active substances which quantity or strength lower that the minimum or higher than the maximum standard (20%).' Substandard drugs are '...drugs produced so that their purity or other characteristics which are important to their quality differ from the standards prescribed in the registered formula…'

Table 19 Official definitions of poor-quality medicines in each country

This research also underlies the value of exploring perceptions of a policy issue to understand variations in policy developments and implications for cross-sectoral and cross border cooperation. As previously argued, the definition and interpretation of a policy problem forms part of its drivers and its solutions (Parsons 1995). Understanding how the problem of poor-quality medicines is framed across the three countries and between categories of respondents, informed my analysis of policy responses to improve access to quality medicines. The dominant frames across institutional and national settings were the security, the health systems

and the regulatory frames. Despite the salience of these three frames, each is articulated differently between policy actors Cambodia, Laos and Thailand.

Frame	Security	Health Systems	Regulatory
Cambodia	Migration	Access to Medicines	Enforcement capacity
	Drug-resistant malaria	Unlicensed outlets	Stakeholder cooperation
	Regional Threat		
Laos	Victim of smuggling	Access to Medicines	Enforcement capacity
	Geographical position	Poor infrastructure	Stakeholder cooperation
		Inequity in access to health services	
Thailand	Migration	Access to medicines and e-pharmacies	Post-marketing surveillance capacity
	Regional threat		Stakeholder cooperation
	Organized Crime		

Table 20 Summary of main themes for each dominant frame across the three case country studies.

As demonstrated in the results chapters (6-8), both government and non-government respondents developed county-specific themes in their interpretations of the challenge of poor-quality medicines within these frames (See Table 20, page 225). Although the security paradigm appears to be the dominant one, there is rarely just one paradigm at work (Rushton & Williams 2012). Beyond these three dominant frames, I discuss relevant findings under the three other frames: the political, medical and economic frames. The thematic variations within these frames also serve to differentiate how the challenge of poor-quality medicines is understood across institutional and national settings, and inform my observations on prospects for the coordination of regional policy responses (in section 9.4).

9.1.1 Security frame

9.1.1.1 Securitisation of health issues

The dominant frame among government level respondents across the three national settings was the security frame. This was apparent in the repeated language used around the policy issue as a 'threat' or a 'danger'. The use of terminology by government respondents represents an obvious speech act of securitization (Balzacq 2010). It was also apparent in the way that

anecdotes that were provided, which illustrated the sources of this threat by referencing the 'threat' of migrant worker movements in border areas and the increasing cross-border movement of illegal goods including medicines. The security frame was prevalent because of the perception of importance attributed to these policy themes. Despite variations in the sub-themes emerging from under this frame in Cambodia, Laos and Thailand (see Table 20 page 225), the securitisation of this policy problem by government-level respondents was common to all interviews, irrespective of the national context. The securitisation of the problem of poor-quality medicines among government-level respondents in Cambodia, Laos and Thailand also occurred around drug-resistant malaria, which was perceived to be a threat to malaria elimination efforts. Drug resistant malaria was interpreted as more than a medical concern, but as a national threat to the wellbeing of populations, both nationally and beyond borders. This study suggests that the securitisation of drug resistant malaria as a health security issue has had important policy outcomes; such as in Cambodia with the successful enforced ban on Oral Artemisinin Monotherapies (oAMTs). It has triggered policy action and the dedication of resources to initiatives aimed at reducing access to unauthorised AML treatments, which contributed to better access to quality-assured ACTs.

Traditionally, a security concern is seen as a threat to the integrity of a territory and material stability of a nation (McInnes & Lee 2012). Beyond the traditional conception of military threats, health policy issues have been identified as non-traditional sources[53] of insecurity since the 14th century. The initial focus of health security was on the challenge infectious diseases (Ooms & Hammonds 2016; McInnes & Lee 2012b), such as the plague epidemic, which were recognised to pose immediate risks to both poor and wealthier nations and communities (Ooms & Hammonds 2016; Labonté & Gagnon 2010). The influenza epidemic, for example, was among the first global health issues framed as a health security threat by the global community (Rushton & Williams 2012). Factors contributing to non-traditional security threats – such as the dynamics of migration, smuggling or the economic gap resulting in poverty (Emmers 2007) – have been identified by respondents as determinants of the problem of poor-quality medicines. This explains their perception of the problem of poor-quality medicines as a health security threat. Global health security issues may also be perceived as threats to the social wellbeing of populations, beyond an individual or a single community (McInnes et al. 2012). As seen in the case of anti-microbial resistance, framing a health issue as a security concern for the wellbeing of the population helps to raise political interest and to mobilise both human and financial resources towards a coordinated response. This was

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[53] Non-traditional security issues relate to the social, economic and political wellbeing of populations, rather than the defence of territorial integrity.

demonstrated by recent debate around the issue of antimicrobial resistance, particularly in the United Kingdom. Evidence of AMR as a threat to the wellbeing of populations across borders has triggered high-level interest in addressing this issue (O'Neill 2016). For this study, the results from the interviews demonstrate the securitisation of poor-quality medicines.

9.1.1.2 National security threat

As Entman (1993) suggests, frames are also defined by what they leave out. Under the security frame, government respondents from the three countries rarely define the security threat posed by poor-quality medicines as a global threat, but rather as a national security threat. This suggests an initial process of localization of the policy goal of access to quality medicines that responds to their national interests and political values, an essential precondition according the Acharya (2009) for the effective and gradual adoption of a policy goal. These national interests and concerns include, for example, the protection of populations against disease as well to economic wellbeing. As Labonté & Gagnon (2010) suggest, the security frame is triggered when national economic or political interests are engaged. For example, Thailand explains that poor-quality medicines pose a threat to the domestic pharmaceutical industry, including the sale of pharmaceuticals through online pharmacies, which are perceived as hard to regulate. Here, results suggest a blending of both the security and the economic frames. Smuggling of illegal goods (narcotics as well as poor-quality medicines) is perceived as a threat to the Thai and Lao economy, especially because of Laos' geographical position as a transit land-locked nation. Respondents described the problem of poor-quality medicines as a threat *from* the region, coming from neighbouring countries and amplified by the cross-border movement of people and goods. Authors argue that the process of securitisation through framing of a global health issue is a political act and does not always reflect reality (Balzacq 2010; Balzacq 2005). The securitisation of the problem of poor-quality medicines as national security threat coming from neighbouring countries, strategically shifts the responsibility for addressing the problem beyond the national government.

9.1.1.3 The success of the security frame

The security frame emerged as the dominant frame arguably because of its flexibility and its adaptability to different contexts and their varying structural factors. The security frame was predominant because it aligns with the medical, as well as the economic frames. It was also particularly resonant among policy actors because it draws on the material world (McInnes & Lee 2012a); both the reality of migratory movements in the region and the emerging threat of

artemisinin-resistant malaria. The security frame therefore encompasses policy actors' concerns around drug-resistant malaria as expressed under the medical frame. The security frame also bridges onto the economic frame – as demonstrated in Thailand, for example – where the threat of poor-quality medicines was perceived as a threat to the domestic pharmaceutical industry. Similarly, in Laos, respondents referred to a changing economic landscape of the Mekong region, the nature of regional investments and widespread money laundering activities, as creating a climate of fear and triggering the national security frame. Government respondents in Laos mentioned the threat of regional trade imbalances as rendering an economy that struggles to 'keep up' with its neighbours, even more vulnerable. This point was reinforced by expert respondents who commented on the general landscape of the region. In blending the security and the economic frames, respondents discussed issues of poverty and the welfare of their citizens as a threat to the integrity of the state. The security frame also resonated across borders because of its allusion to the context of trade between Mekong countries and the perceived challenges of the ASEAN Economic Community 2015, which has called for the reduction of barriers to trade between Southeast Asia Nations.

9.1.1.4   From drug safety to drug security

Despite the salience of the security frame across national settings, Thailand, Cambodia and Laos' policy responses focus predominantly on addressing the threat of substandard medicines, omitting specific responses to drug falsification as an international criminal act. Results suggest a stronger focus on improving 'drug safety' rather than 'drug security'. Drug safety relates to the protection of consumer health, the safety and efficacy of medicines and focuses on strong pharmacovigilance and adverse drug reporting systems (Hornberger & Cossa 2012). Drug security, other the other hand, encompasses strategies to combat the circulation of counterfeit or falsified medicines (Hornberger & Cossa 2012). Drug security goes beyond drug safety to include a criminal law dimension. Policy efforts to improve drug security would, therefore, require the cooperation of law enforcement officials.

Why the securitisation of this issue has not translated into a robust policy response beyond drug safety, is an interesting question I reflect on throughout this chapter and which could form the focus of further study. The securitisation of the problem of poor-quality medicines is not reflected in current legal frameworks. Countries currently rely on trademark laws to address the problem of falsified medicines as those are better defined (Attaran 2015a). The limitation of that is it favours the protection of trade interests over public health concerns. At a workshop on Medicine Quality held at the London School of Hygiene and Tropical Medicine in 2015,

Professor Philippe Guérin from Oxford University suggested the need for countries to broaden their definitions of the problem of poor-quality medicines (Guérin 2015). Arguably, this broader understanding should extend beyond the concept of drug safety to that of drug security. Experts agree that criminal law should be invoked to address the problem of poor-quality medicines, which equates to 'attempted murder' (EXP29_Pharma20160623). Experts also pointed to a need for to a clearer global definition of the international pharmaceutical crime of falsification as a security threat, and subsequently a differentiation of offences for the production, sale and circulation of substandard and of falsified medicines to improve both drug safety and drug security[54].

9.1.2   Health systems frame

The health systems frame was another common frame across all three case countries, more specifically from the accounts of non-government respondents. The latter respondents perceived the problem of poor-quality medicines as linked to poorly resourced health systems. This frame was particularly resonant in Cambodia and Laos, where respondents regularly pointed to the poor state of health infrastructure (Laos) and the poor access or limited use of public health services (Cambodia). Under the health systems frame, respondents highlighted challenges in terms of the procurement, distribution and dispensing of medicine. For example, they explained that poor-storage conditions and recurrent stock-outs were still an issue, especially in peripheral areas. An expert respondent from the GF noted that cases of stolen or diverted AML stocks are still a risk (EXP25_INGO20150930). As an additional challenge, out-of-pocket payments remain high, especially in Laos, driving a demand for cheaper medicines, which is said to fuel the market for cheaper, potentially poor-quality medicines. The large amount of unlicensed private outlets selling medicines is yet another challenge mentioned. This problem bridges onto to the regulatory frame, as it is linked to the perceived poor enforcement of licensing procedures from the National Regulatory Authorities (NRAs). Patient health-seeking behaviour, the tendency for patients to self-diagnose and self-treat and to purchase medicines from unlicensed drug vendors, is yet another health systems challenge.

Despite these common themes, there are variations in the articulation of this frame between the three countries that draw on the specificities of each national context. Respondents in Laos referred to the inequitable access to medicines for vulnerable populations. In this regard, Lao respondents framed the problem of access to quality medicines as a blend of health systems and economic challenges, since vulnerable populations live in more remote areas and often

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[54] Prof Amir Attaran proposes a model law to this effect, where drug falsification is elaborated as a crime rather than as a regulatory offense (Attaran 2015b; Attaran *et al.* 2011).

live in poverty. Accessibility to public health facilities in Laos is compromised by the country's mountainous nature and size, and its poor road infrastructure – making some peripheral areas inaccessible for replenishing medicine stocks during the rainy season. In Thailand, respondents emphasized the challenge of access to public health facilities and to subsidized medicines at border areas, and among Mobile Migrant Populations (MMPs) more specifically. Due to its economic status as an upper-middle-income country, experts suggested that Thailand has faced increasing international pressure to strive towards Universal Health Coverage (UHC), prompting policy efforts to extend UHC to MMPs in 2002 (EXP10_Academia20150303). In Cambodia, the proliferation of unlicensed private sector outlets was noted as a health systems challenge, explained in part as a consequence of poor confidence in the public health system, which suffered during the Khmer Rouge era and has undergone a slow recovery since. Despite a social marketing program in place since 2004 which has improved access to quality ACTs, stocks-outs of ACTs remain an issue as reported in 2011 by Shunmay Yeung (2011) and confirmed by respondents in Phnom Penh. Additionally, complex networks of wholesalers and pharmacy outlets also makes the supply chain difficult to monitor (Patouillard *et al.* 2011).

9.1.2.1   Access to medicines from a health systems perspective

The themes under the health systems frame support the wider paradigm of access to medicines from a health systems perspective, as introduced in the ATM model first detailed in Chapter 3. Respondents share a wider interpretation of access to medicines that extends beyond the current global focus on access to *affordable* medicines, which translates into a constant pressure to produce low-cost medicines. AMLs, being available for free or at a subsidized price, are not directly affected by issues of affordability. Instead, results suggest a wider focus on improving access to medicines which should encompass health systems strengthening efforts. Respondents argued that the 4As of access to medicines – availability, accessibility, acceptability and affordability – are dependent on adequate health infrastructure, resources and information. These elements all contribute to effective health service delivery. By blending the health systems and economic frames, respondents in Laos acknowledged the impact of economic factors on access to medicines. Respondents across the three countries also recognised the underlying importance of individuals and communities; and of understanding their health seeking practices and cultural preconceptions of medicine quality. These are important elements in understanding health systems challenges in terms of access to medicines, which are still largely under-explored across national settings.

Respondents do realise that the policy goal of improving access to quality essential medicines (beyond AMLs), is only possible if it is coupled with efforts to strengthen the health system. Advocating for health systems strengthening is seen by non-government respondents as a trigger for reforms to improve equitable access to quality health services for all, and to quality medicines across all therapeutic drug categories, not just AMLs. The health systems strengthening approach may also be perceived as one angle on which to motivate government reforms to protect nations against emerging and re-emerging diseases, as well as to mitigate the potential negative impact of increased trade, the rising movement of goods and people, and of inequitable growth.

9.1.2.2   Human security

The results of this study suggest that the health systems frame extends onto the security frame, by combining the health and human security concepts. The health systems frame encourages a process of wider frame reflection[55] on the concept of security (to human security) and on the need to acknowledge system gaps and to strengthen the system to improve access to quality medicines. Human security is understood as freedom from need and from want and, since its first 1994 definition by UNDP, includes health as one of its inherent components. Health policy issues have also been framed as human security concerns when they are perceived as a threat to a population's welfare and threats to a populations' freedom from want or fear (McInnes & Lee 2012b). Respondents in Laos alluded to this paradigm regularly when referring to inequity, poverty, the high out-of-pocket payments, and poor health infrastructure especially in the remote and mountainous areas of the country – as well as to the poor access to quality and affordable medicines through public health services as a result. The concept of the right to health which underpins this frame, therefore, acts as a value-driven principle to improve access to good quality medicines and supports the policy goal of ATM. Respondents also acknowledged that the right to health can only be achieved by strengthening health systems (Hammonds & Ooms 2014). This frame, and how it relates to human security, explains how the securitisation of the problem of poor-quality medicines prompts a debate on the need to strengthen health systems to reduce inequalities and improve access to medicines for all.

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[55] As explained in Chapter 4, 'frame reflection' is a process by which frame sponsors question or review how an issue is interpreted in response to policy controversies (Schön & Rein 1994). Frame reflection occurs within processes of frame competition or in response to competition from different framings of a similar issue, promoted by other frame sponsors.

9.1.3   Regulatory frame

9.1.3.1   Frameworks

Government and non-government level respondents across the three countries framed the problem of poor-quality medicines as a regulatory challenge. Under this frame, respondents alluded to the inadequate nature of the existing regulatory frameworks; namely, the lack of clear definitions and commensurate penalties against the production, sale or distribution of substandard or falsified medicines. Despite the common viewpoint among respondents in Thailand that the Thai drug regulatory system is more robust than that of its neighbours, there remain notable loopholes in Thailand's pre-marketing system (e.g., the lifelong registration of medicines), as well as post-marketing surveillance framework (e.g., the unsystematic sampling of essential medicines including AMLs in peripheral areas). Thai respondents also noted that the current regulatory framework fails to address the emerging threat posed by the proliferation of online pharmacies. Regarding the distribution and sale of medicines at points of sale, various respondents across the three countries referred to the distribution practice of cocktails of drugs and the lack of enforcement of prescription requirements. Experts also noted the general inadequacy of existing post-marketing surveillance frameworks across the Mekong, as confirmed by non-government level respondents in the field. Furthermore, experts noted that the limitations of current regulatory frameworks, besides the lack of coherence in the legal definitions of poor-quality medicines, is that there are no adequate legal frameworks to address drug security – or the threat of falsified medicines and a crime.

9.1.3.2   Capacity and enforcement

In Cambodia and Laos specifically, respondents alluded to issues of capacity and capability to regulate poor-quality medicines. In Laos, respondents pointed to weak technical capability and capacity in the drug testing laboratory, as well as poor financial and human resources to support capacity development. In contrast, in Cambodia respondents placed more emphasis on the lack of financial resources. The lack of funding for regulators has repercussions on the availability of human resources, as many trained regulators are tempted to move to the private industry. Despite the existence of cross-sectoral mechanisms for cooperation against poor-quality medicines in Cambodia and Laos, respondents noted that these bodies are not supported by commensurate or sustainable funding.

Although surveillance capacity for the quality of AMLs has improved with technical assistance from international partners such as USP, gaps in human, technical and financial resources

make enforcement of existing rules and regulations to control the supply chain of pharmaceuticals challenging. An expert respondent stated that 'most of countries claim to have comprehensive regulation on medicines and have law[s] on paper…but the enforcement part is missing.' (EXP17_INGO20150716). In Cambodia, the problem of unlicensed outlets is partly due to the poor enforcement of licensing procedures. Non-government respondents explained that regulators are not incentivised to prioritise the enforcement of sampling procedures to verify the quality of essential medicines, as their salaries are too low in relation to the large scope of their activities. Existing mechanisms are not always implemented adequately due to insufficient staff and the over-stretched mandates of regulators and inspectors. In Cambodia, inspectors have operational and regulatory tasks that stretch from the control of food products to medicines. Respondents also mentioned that regulators are tasked with monitoring the compliance of numerous regulatory functions without the power or mandate to seize stocks or to close outlets. This largely limits their capacity to enforce guidelines independently and effectively, and precludes a strong coordination of efforts with law enforcement agencies. As the results suggest, however, this coordination is not always systematic, due to a lack of awareness among law enforcement officials of the problem of poor-quality medicines.

The variations in how poor-quality medicines are defined in official documents, as well as the varying levels of capacity to regulate and enforce rules and regulations along the pharmaceutical supply chain, leads to many different standards of quality (Ravinetto *et al.* 2016; Caudron *et al.* 2008). The imbalance in regulatory capacity between countries in a region, fuels the flow of medicines across borders. The lack of regulatory capacity is also intrinsically linked to weak health systems and results suggest that the regulatory and health systems frames overlap on various themes. This could explain the combined salience of these two frames across the three countries. This study suggests that strengthening health systems is only possible if the right rules and regulations are in place and if they are adequately enforced. The regulatory frame also bridges onto the political frame, whereby weak transparency and poor accountability of regulators is perceived as impeding the effective enforcement of regulatory provisions for access to quality medicines.

9.1.4 Political frame

9.1.4.1 Governance

The issues raised by policy actors under the political frame extend to the three salient frames described above, namely: the security, health systems and regulatory frames. In all three

countries, non-government respondents alluded to political and governance issues as hindering the enforcement of regulations to improve the quality of medicines. The level of political priority attributed to the problem of poor quality medicines impacts the level of efforts and resources dedicated to addressing it. In Thailand, respondents explained that malaria was no longer considered a political priority due to the low burden of the disease in central areas of Thailand. This impacts the level of effort and resources dedicated to the sampling and quality testing of AMLs by the Thai Food and Drug Administration and the Bureau of Drugs and Narcotics. In terms of prioritisation of efforts, law enforcement officials in Thailand also explained that customs and police officials are held accountable for their efforts against the illegal smuggling of narcotics. The narcotics trade has been a long-standing policy priority in Thailand, backed by a strong system of penalties and clear implementation procedures. Law enforcement respondents explained that this leads to the prioritisation of efforts against the narcotics trade rather than the circulation of poor quality medicines.

Respondents also explained that weak enforcement is a wider governance issue linked to ineffective de-centralisation of regulatory functions, as well as instances of corruption and vested interests. Under this frame, government-level respondents described the uneven enforcement between central and the peripheral areas as a challenge to effective regulation against poor-quality medicines. This is perceived to be a result of poor cross-sectoral cooperation and the inefficient delegation of inspection responsibilities to regulators in provincial health offices. The uneven enforcement of rules and regulations was perceived as especially problematic in Laos, where access to remote areas to monitor implementation is particularly challenging. Under this frame, non-government respondents in Cambodia also explained that regulators' capacity to inspect pharmacy outlets or warehouses impartially is potentially compromised by regulators' vested interests in the industry. Non-government respondents alluded to a lack of transparency on data around poor-quality, leading to inaccurate interpretations of this policy problem in Cambodia and Laos. Non-government respondents also referred to the un-transparent management of funds in Cambodia and Laos. The few government-level representatives interviewed in Cambodia held a very different perspective from non-government partners. The results demonstrate that poor governance and lack of transparency impedes countries' capacity to enforce existing regulations effectively to improve ATM.

9.1.4.2 Responsibility and Accountability

Under the political frame, respondents also mentioned issues of responsibility and accountability of national regulators. Perceptions of the policy problem of poor-quality medicines influences *who* local policy actors considered as responsible. For example, government level respondents evoked the problem of poor-quality medicines as a threat *from* the region, actively shifting the national responsibility for the circulation of poor-quality medicines towards neighbouring countries. Responsibility is either placed on neighbouring countries, or on the consumer for purchasing medicines from unlicensed vendors. Despite a strong awareness of the threat of poor-quality medicines, there is an apparent lack of responsibility-taking around this policy challenge, demonstrated across the three national settings. This lack of ownership of the responsibility for the circulation of poor-quality medicines could explain the weak implementation of existing measures to regulate the quality of medicines. These observations link with the main observations made under the security frame across the three countries. It appears that the concept of security acts as a wider 'ideational paradigm' (Rushton & Williams 2012; Acharya 2009; Payne 2001), that is used here as a vehicle to shift responsibility away from the national government and to neighbouring countries. This reference to responsibility suggests a blend of both the security and political frame.

The securitisation of a policy issue is an inherently political process which can only be interpreted within a political context (Balzacq 2005), hence the importance of considering the themes under the political frame for my analysis. The political context is an important factor in the attribution of responsibility for a policy problem (Iyengar 1991). Non-government respondents explained that political commitment to address the threat of poor-quality medicines remains superficial. There are few mechanisms to hold regulators accountable for the enforcement of measures against poor-quality medicines, and insufficient capacity among regulators to take on the responsibility of this task. Moreover, the problem of poor-quality medicines remains a politically sensitive issue. Government respondents in Cambodia, for example, expressed concerns with regards to eroding confidence of its population in the public system, driving a desire to highlight successful policy moves and to frame the threat of poor-quality medicines as coming from beyond Cambodia's borders. In Cambodia, government level respondents showcasing efforts on the ban on oAMTs, drew attention to what they perceived as the positive work of regulators and inspectors. In parallel, it diverts attention from the weaker regulatory areas in the system, such as post-market surveillance activities, for which regulators are not held accountable. As the results under the political frame demonstrate,

policy actors' perceptions of the problem of 'poor-quality' medicines are context-bound and relate both to political interests, fears related to national security and to trust in the public health care system.

9.1.5 Medical frame

While the medical frame was not the most salient among respondents, it does explain the challenges of expanding discussions on the problem of poor-quality medicines beyond antimalarial medicines or beyond the challenge posed by substandard medicines exclusively. Under the medical frame, respondents place more emphasis on improving drug safety over drug security, with a focus on pre-marketing regulatory functions as well as pharmacovigilance and adverse drug reporting (Hornberger & Cossa 2012). Drug Safety does not encompass efforts against falsified medicines from a criminal law perspective (as detailed in section 9.1.1.4). The focus on drug safety over drug security when discussing the threat of poor-quality medicines suggests only a partial understanding of the policy goal of improving access to quality medicines, addressing the threat of substandard over that of falsified medicines. Respondents emphasised the threat of poor-quality medicines, including unauthorised oAMTs drug safety and patient protection. In all three countries, government-level respondents steered discussions around poor-quality medicines towards policy efforts to monitor the quality of medicines as conducted under the national malaria programs. The problem of poor-quality AMLs was framed as a concern for malaria elimination, exacerbated both by the continued circulation of oral artemisinin monotherapies (oAMTs) and of poor-quality antimalarials (AMLs). Evidence of drug resistant malaria triggered policy actors to recognise the threat posed by poor-quality AMLs and to acknowledge the importance of the policy goal to improve access to good quality AMLs. This concern drives efforts to improve the rational use of medicines and to enforce the ban on the sale and distribution of oAMTs to improve access to effective treatments and to support malaria elimination efforts. Respondents rarely referred to whole system efforts to improve ATM for all categories of medicines. Government-level respondents in particular, were less keen on discussing medicine falsification as a crime and seemed more comfortable expanding on the irrational use of medicines for the treatment of malaria. This might explain why, despite the securitisation of the problem of poor-quality medicines, efforts to improve ATM are focused on drug safety rather that drug security.

Results under the medical frame also suggest that conceptions of medicine 'quality' are context and culture-bound. In Thailand, for example, respondents from government and academia first described the threat of poor-quality medicines largely as a 'contamination' issue affecting traditional health supplements. Seeing as the use of traditional remedies is actively promoted

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by the Ministry of Public Health in Thailand, this was presented as a major drug safety issue and a concern to consumer health. It is likely that these different concepts of medicine quality itself, have influenced the variations in interpretations of the problem of poor-quality medicines across national settings. Yet again, this observation is mitigated by the fact that the conceptions of quality introduced above are bound to the English translations of original definitions.

9.1.6 Economic frame

Various themes under the economic frame were invoked in line with the securitisation of the problem of poor-quality medicines. This frame was more resonant among Thai and Lao respondents – and articulated differently in both settings. Thai respondents insisted on the threat of poor-quality medicines for the domestic pharmaceutical industry – a national threat to the Thai economy. This could explain the Thai FDA's focus on controlling pharmaceutical advertising, improving the rational use of medicines to prevent purchases from online pharmacies and its active engagement in strengthening Good Manufacturing Practices (GMP), as well as GMP compliance in the region through region-wide standardisation. In Laos, respondents highlighted that poverty, exacerbated by economic disparity and inequitable growth between Laos and its immediate neighbours, impacts access to affordable, quality medicines in Laos – particularly for the more remote communities where the health infrastructure is weaker. In both countries, however, respondents described regional investments and the disparity that these investments perpetuate in the region, as a factor contributing to the circulation of poor-quality medicines and exacerbating the trade in illegal products in general. Laos respondents referred to Chinese investments including in private hospitals, as a challenge to the effective regulation of the entire supply chain of medicines in the country; seeing as Chinese-run hospitals were procured through a parallel system exempt from local inspections. More specifically, the liberalisation of trade and the introduction of the ASEAN Economic Community raised concern among government respondents regarding the increased movement of goods and people, and the repercussions this could have on the circulation of falsified or substandard medicines. This regional economic trend is picked up on by experts as an added challenge for the effective regulation of pharmaceutical supply chains in Southeast Asia (EXP18_Academia20150407; EXP09_Donor20150224). For this reason, it is important to be aware of the political economy of the region to understand how the problem of poor-quality medicines is perceived.

9.2   Frame sponsors

Different configurations of policy actors and policy networks promote the six frames detailed in this research and actively shape the processes of policy reform and development. This section explores who these frame sponsors are and how policy communities and networks contribute to these framings. Policy actors are leaders (or sponsors) (Schön & Rein 1994) in a process of frame competition and alignment, whereby each policy community influences policy choices and decisions by promoting a specific standpoint or policy image of the threat of poor-quality medicines. In this regard, they act as 'policy entrepreneurs' (Kingdon 1995). These policy actors have varying levels of authority and power in influencing the policy process, which explains how and why certain frames prevail over others.

9.2.1   Power and actor interactions

The salience of a frame depends on a process of political negotiation between policy actors (Payne 2001 p. 44). While NRAs are ultimately responsible for formulating new policies and for implementing rules and regulations for drug quality control, results suggests that different policy actors have brought the issue of poor-quality AMLs to the attention of NRAs. Policy interactions actively shape the process of issue and interest formation among regulators and around the policy goal of access to quality medicines. NRAs and ministries of health then agree on definitions of poor-quality medicines and the penalties incurred for non-compliance of regulatory guidelines. They guide the policy making and revision process around the regulation of pharmaceuticals.

'Issue communities' (Marsh 1998, p.15) in which actors exchange viewpoints on a policy issue, facilitate a process of frame reflection. These issue communities provide a space to debate a policy issue and present policy choices. Policy interactions across a variety of institutional settings – from government to academia or industry – influence framings of a policy issue, as well as the process of policy formulation. In Thailand, trade and industry representatives are actively involved in the reform process of rules and regulations for pharmaceuticals, as seen in chapter 8. These actors participate in the policy formulation and negotiation process through formal consultations with drug regulators, and within a wider network of cross-sectoral communication. In Cambodia, for example, the IMC has been a useful network for ministry representatives across sectors to gain awareness about the issue, and to deliberate on roles and responsibilities for addressing it. The IMC has played an important role as a network to mobilize efforts to enforce the ban against oAMTs. A Memorandum of Understanding (MoU) to fit a similar purpose between nine ministries in

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Thailand, may have worked to encourage continued consultations between key stakeholders. However, it is unclear from the results whether the MoU has led to specific policy outcomes. Nevertheless, results suggest that the structures for formal cross-sectoral consultations and interactions are stronger in Thailand, where regulators from the Thai Food and Drug Administration engage with the industry and with academia on a regular basis.

Results also suggest that the frequency of interactions through specialized committees, such as the IMC, supports the process of adoption of the ATM policy goal (Cortell & Davis 2000). Such structures can also facilitate the clear division of roles and responsibilities and checks and balances, as demonstrated in the case of Thailand. Respondents in Laos and Cambodia, on the other hand, where interactions between regulators and other policy actors remain ad-hoc, still report issues in terms of division of roles and responsibilities, which in turn impedes the effective enforcement of rules and regulations. Where policy networks are not institutionalised, the debate around ATM remains more sporadic. The closer a policy actor is to the policy making circles the more influence this actor may have on the adoption of a policy goal (Stoeva 2013, p.37), and policy networks facilitate this repeated proximity to policy makers.

This study demonstrates that epistemic communities (networks of experts and representatives from academia) also play an active role in shaping the process of interest formation, by making compelling evidence of the risks of poor-quality medicine available to regulators. In Laos, the Lao-Mahidol Oxford Tropical Medicine Research Unit (LOWMRU) plays an important role in the promotion of the ATM policy goal, by engaging with policy makers and supporting the sampling and evaluation of drug quality for the NRA. Regulators in turn demonstrate an openness to operational research and evidence-based policy reforms. The role of academia in interest and policy formulation was also noted by Thai respondents. The literature on policy making in Southeast Asia confirms that epistemic communities play an important role in driving policy coordination in Southeast Asia (Acharya 2009, p.29; Woods 1993). Academia plays an important role, therefore, in influencing policy choices in response to poor-quality medicines.

Networks of policy actors appeared to be more inclusive of different sectors and institutions operating in Thailand, actively involved members of both academia and the pharmaceutical industry in processes of policy reform (such as for the New Drug Act 2003). Through these networks, the pharmaceutical industry has a strong voice in promoting the ATM policy goal. Respondents in Thailand frame the problem of poor-quality medicines first and foremost as a

threat to the domestic pharmaceutical industry and its healthy growth. The securitisation of the issue of poor-quality medicines triggers a different combination of policy actors in Thailand, including industry representatives. This is in line with the comparatively dominant focus of trade interests in the policy response to poor-quality medicines.

Policy networks, therefore, play an active role in the elaboration of a security construct. As Caballero-Anthony & Amul note: 'securitizing health involves not only the use of speech acts but also the building of political networks and the implementation of relevant policies' (2015, p.32). The securitisation of a policy issue is a political act driven by policy communities that set political agendas according to their political interests and priorities (McInnes & Lee 2012b, p.133).

9.2.2   International policy actors

Results demonstrate that policy actors within NRAs have also been influenced in a process of frame reflection by international partners, including technical agencies for capacity building, and donor organisations. The USP and PSI, as technical agencies and implementing partners on the regulation of pharmaceuticals have, since the early 2000s, influenced regulators' perceptions of the importance of the problem of poor-quality AMLs, by highlighting the risks associated with drug resistance. These agencies have also encouraged efforts to improve the supply of good quality treatments through various policy options, including the Public-Private Mechanism to distribute AMLs through licensed private sector outlets in Cambodia.

International organisations in global health can have a significant influence on the pathways of policy response as demonstrated in the case of HIV/AIDS, when advocates successfully raised the fight against HIV/AIDS to the highest political agenda, mobilising funds to support countries in their implementation of policies for improved access to affordable antiretroviral treatments globally (Rushton 2012). Results also demonstrate that donor-organizations in the malaria space have a strong influence on the policy agenda for drug regulation through the prism of infectious disease control and elimination. International non-governmental agencies such as the WHO and donor organizations such as the GF, have actively driven the agenda for malaria elimination in the Greater Mekong Subregion. This is apparent through the normative influence[56] of strategic documents by WHO, such as the Strategy for Malaria Elimination in the Greater Mekong Region 2015-2030 (WHO 2015) supplemented by the Global Technical

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[56] As an international agency, the WHO has the normative power to guide policy action and continues to promote efforts towards achieving universal health coverage, the right to health and improving access to medicines.

Strategy for Malaria 2016-2013 (WHO 2015a). The GF's Regional Artemisinin Resistance Initiative (RAI) also encourages active quality monitoring of antimalarial medicines to reduce the risks of drug-resistant malaria spreading in the GMS. Funding for malaria elimination and artemisinin resistance containment has shaped policy negotiations and reforms to some extent, especially in under-resourced regulatory settings where external support from aid organizations is pivotal to the support health systems strengthening efforts. In a process of frame reflection, this may have influenced regulators to dedicate time and resources to quality monitoring efforts that also support the malaria elimination agenda – for instance, the enforcement of the ban on oAMTs, to showcase.

A representative from a development aid organization in Cambodia discussed the difficulty of competing policy priorities in a crowded landscape of international partners and donor organizations. The respondent cited the example of WHO's ERAR and the operations funding under the GF's RAI grant (announced only a few months after ERAR). Both initiatives aim to reduce the spread of drug-resistant malaria while indirectly supporting efforts for access to quality AML treatments. Experts added that while all three countries studied are signatories of the Paris Declaration on Aid Effectiveness, which advocates for the coordination of aid efforts to avoid duplication and maximise efficiency of outcomes, the landscape of international donors remains chaotic. The crowded landscape of initiatives to improve access to quality AMLs is therefore largely donor-driven, with a strong incentive to focus exclusively on antimalarial medicines through parallel mechanisms for AML quality monitoring. Arguably, the focus on antimalarial medicines, while it represents a successful entry point to the policy goal of ATM, does not encourage efforts to strengthen the drug regulatory system at large – to encompass all categories of essential medicines at risk. This impacts the sustainability of efforts to improve drug quality monitoring processes. The ATM policy goal for essential medicines remains only secondary to that of drug-resistant malaria elimination.

9.3 Pathways of policy response

The way policy actors frame a policy issue precludes certain pathways of response over others (Schön & Rein 1994), and policy actors' framings of the challenge of poor-quality AMLs in Cambodia, Laos and Thailand have generated different pathways of policy response. To explain the formulation and reformulation of policy solutions, it is crucial to consider the processes of frame alignment and the influence of key focusing events. In this section, I explore the implications of framings of the policy problem and of contextual factors for policy developments across the three national settings. I reflect on how perceptions of the problem might have shaped the adoption of the ATM policy goal, that is when the policy goal has been

recognised by policy makers (e.g., the ministry of health and NRAs) as being in their interest (Acharya 2009). This occurs when a policy goal is framed such that it resonates with the political priorities of that country.

This policy development process is driven by policy actors, through frame bridging, blending and shifting – all contributing to a process of frame reflection. Different articulations of the six frames around the problem of poor quality medicines have generated different policy proposals and led to different policy developments. As an example: the problem of poor-quality medicines has been officially recognised as a policy *issue* at different intervals in the policy process. Processes of issue formation have been triggered by different focusing events in the three national settings. Issue formation in Thailand occurred between 1991 and 1997, around the challenges related to access to medicines for marginalised populations, and the emergence of drug resistance at border areas. This prompted initiatives to improve universal health coverage for better access to quality assured medicines through the public health system (between 1997 and 2002). Issue formation around the challenge of poor-quality AMLs occurred at a later stage in Cambodia and in Laos, largely steered by technical development partners including the USP and the WHO in both countries. Results suggest that in both cases, evidence of drug-resistant malaria in border and forest areas triggered the interest of policy actors. This may have prompted the establishment of the IMC in Cambodia in 2005, for example. Evidence of drug-resistant malaria as a threat to national malaria control efforts has added pressure on ministries of health and drug regulators, prompting a process of frame reflection whereby government level respondents evoked the security frame to define the challenge as a national security concern. This may have been the trigger for policy revisions (such as for example the 2011 amendment to the Law on Drugs in Laos), which prompted changes in the definition or substandard and falsified medicines and in how the problem of poor-quality is framed.

9.3.1   Frames and policy outcomes: complex causality

Despite the above observations, my findings indicate no clear and direct causal link between framings of the issue of poor-quality medicines and policy responses to address the policy problem of poor-quality medicines. Framing analysts such as Gusfield (1991) or Jasanoff (2005) have argued that framings influence pathways of policy response. Others have demonstrated the impact of global frames on global health policy processes (Kamradt-Scott & McInnes 2012; Reubi 2012; Williams 2012). The body of literature on framing analysis suggests that framing analysis is useful to identify linkages between ideas and policy processes when interpreted along a framework of policy analysis (Koon et al. 2016). The interpretive

framing analysis approach adopted for this study suggests however that the causal link between framings of the policy issue of poor-quality medicines and the policy response in the three case studies is not linear or one dimensional. This is apparent in that despite the securitisation of poor-quality medicines as a policy issue among government-level respondents, there is limited evidence of policy efforts beyond drug *safety*, towards a policy response that addresses drug *security* against falsified medicines through systematic cooperation with law enforcement agencies and the judiciary.

Instead, findings demonstrate that the mechanisms by which frames impact policy making processes are more complex than previous research and framing analysis studies might suggest. The results of this study suggest that the relationship between frames and policy outcomes should be interpreted in line with several intervening variables including the broader policy context as detailed in the next section 9.3.3. To evaluate the relevance of a frame and its influence on policy developments, a thorough understanding of the institutional and structural arrangements at the national level is necessary. The findings demonstrate the importance of studying the influence of frames on policy responses through policy communities of actors and the interactions among the main frame sponsors. The case of Cambodia and the Inter-Ministerial Committee is one example of an institutional set up through which measures to improve drug safety against drug resistant malaria were pushed forward, as emphasised under the medical frame. This study also underlies the importance of considering the political economy, as demonstrated in the case of Thailand, where the health systems challenges identified by respondents shape a different policy response unique to the Thai context. In view of its GDP and a developed health infrastructure, Thailand is in a position to prioritise Universal Health Coverage as one way to improve access to quality medicines for all.

The national and regional political context including external focusing events also impact the way that a frame might influence policy processes and outcomes. As will be detailed in the next section, both the evidence of drug resistance and the increasing movement of MMPs at border areas have largely shaped the securitisation of the problem of poor-quality medicines as a national security concern and a threat to malaria elimination efforts specifically. Cambodia being at the epicentre of artemisinin resistant malaria since the early 2000s for example has dedicated much policy attention to reducing the circulation of oAMTs and improving access to quality ACTs for MMPs in border areas in order to contain drug resistant malaria.

The findings also highlight the importance of interpreting frames in terms of their political use by policy actors, and to consider the audience for which they are invoked. Hawkins & Holden (2013) explain that framings can be used as a political tool. Findings suggest that the securitisation of poor-quality medicines as a threat *from* the region and *to* national security may be used as a tool to shift responsibility away from the regulatory authority. The securitisation of the problem of poor-quality antimalarial medicines might also be invoked to align with the broader regional narrative on drug resistant malaria as a security threat used by several international health (including donor) organisations in Southeast Asia.

The results from this qualitative study do reinforce previous work by framing analysts on the importance of considering the various levels of abstraction of a frame. As discussed in Chapter 4, Rein & Schön (1996, p.89) introduce two levels of frames, the rhetorical and action frames. Fischer (2003) explains that framing can serve to reshape a policy problem in how it is diagnosed. Findings suggest that the security frame may have been invoked to strategically reshape the policy issue as a national security concern beyond the responsibility of the state, and attributable to neighbouring countries. As a rhetorical frame, the security frame may also have been imposed by external actors, as an emulation of the global discourse around the security concern posed by drug-resistant malaria and exacerbated by poor-quality antimalarials. This frame may be invoked for the international community in the aim of obtaining capacity building support to address a threat that national regulators do not wish to be held accountable for.

Despite the lack of a direct causality link, it is clear from the findings of this study that studying frames on the problem of poor-quality medicines has been useful to understand parts of the process around the ATM goal. The frames that emerged from the results of this study may not have triggered policy change as would be expected but they help understand the underlying beliefs that could lead to policy change (Béland & Cox 2011; Koon et al. 2016). Results suggest that understanding how ideas are taken up along the policy process (Shiffman 2009), even as rhetorical frames that don't necessarily lead to the matching policy response, is useful to inform future policy developments to address the problem of poor-quality medicines.

> "Framing research does not predict change or advocate for a particular way of seeing the world. Instead, it seeks to provide an explanation for human behaviour in the policy process and how this collectively structures subsequent interactions." (Koon et al. 2016, p.7)

Building on the conclusion by Koon and colleagues (2016) therefore, the analysis of frames in this study accounts for the processes of contestation and the debate of ideas in the policy process around the ATM goal. This next three sections explore this in further detail; from processes of policy formulation to policy developments in context, followed by a reflection on the adoption of the ATM goal as a secondary policy goal.

9.3.2 Processes of policy formulation

To explain what drives the policy development process and how frames may influence policy developments, I refer to March & Olsen's logics of action, namely, the logic of consequences and the logic of appropriateness (March & Olsen 1989, 1998). Both logics are not mutually exclusive and both can explain policy decisions (March and Olsen 1998). Both logics also relate to the notion of actor responsibility to explain policy choices. The responsibility of policy makers is triggered by the material consequences of not acting to protect the security or wellbeing of the nation (logic of consequences). Similarly, policy decisions can be triggered by a sense of duty linked to the normative obligation of striving for the right to health (logic of appropriateness). Both logics can explain the mechanisms by which frames shape policy developments, based on a specific reasoning and cognitive processes.

The 'logic of appropriateness' is triggered when actors take a normative stance which is in line with their preferences and political identity, or because of a shift of political priorities due to an external norm of behaviour. Under this logic, the global policy goal of improving access to affordable, quality, safe and efficacious medicines, as well as the overarching norm of striving towards the right to health, can be a powerful normative incentive for policy change. The logic of appropriateness could explain Thai policy actors' emphasis on Universal Health Coverage to improve access to health services and commodities, including AMLs for all. The logic of appropriateness with regards to poor-quality medicines could also explain the motivation of law enforcement officials to actively participate in INTERPOL's yearly STORM operations against falsified medicines – to be part of a broader movement against international organised crime. However, despite the benefits of such enforcement operations to raise awareness, these operations are one-off interventions with limited long-term and sustainable impact on improving access to quality medicines. Results suggest that the logic of appropriateness is insufficient to explain evidence of weak local ownership of this policy problem across the three national settings. The responsibility to improve regulatory efforts against poor-quality medicines lies in the hands of NRAs and it is the responsibility of the government to protect its population against the threat of poor-quality medicines. As explained previously however, by framing the challenge of poor-quality medicines as a threat *from* the region, policy actors

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choose to shift the responsibility for this policy problem onto neighbouring countries. In light of these observations, I suggest that there is still a need for country-led, sustainable efforts to improve the capacity for continuous monitoring of the quality of stocks of medicines.

The logic of consequences may, therefore, more adequately explain the tendency for policy actors to shift responsibility for the problem of poor-quality medicines. The logic of consequences is based on a cost benefit calculation, when actors agree to a course of policy action because of the consequences of not doing so are greater, or because of the legitimacy gained by adhering to the policy goal. Although the reality of the situation is more complex, my suggestion is that if a policy problem is perceived as a national security threat, the logic of consequences might entice policy actors to take the necessary actions to protect their national interests or that of their population. Following the logic of consequences, the securitisation of the problem of poor-quality medicines could be considered as a strong incentive for policy reform. Under the logic of consequences, states may act because they do not wish to be blamed for not taking any action. This could explain why policy actors frame the ban on oAMTs as a policy success against poor-quality medicines.

The sense of legitimisation from neighbouring countries as important trade partners within ASEAN, might also influence policy decisions. The prestige obtained from being part of a wider movement can drive political will and reform, as well as the fear of 'lagging behind' other neighbouring states or states with similar socio-economic conditions (Rushton & Williams 2012; Towns 2012). Being blamed for inaction or for the mismanagement of donor funds could negatively influence the public's trust and the reputation of the country on the international scene. One anonymous respondent suggested that Thailand may refute the problem of poor-quality AMLs altogether, predominantly because of national pride and the fact that it would not want such evidence tarnishing its image as one of the more developed and upper-middle income countries in the region. This would not be the only potential explanation, however, and an alternative explanation may be that the problem of poor-quality medicines goes beyond countries' means to address the problem effectively, and because admitting to these shortcomings may have broader implications, the least costly policy reaction is to frame it as a threat originating from elsewhere. The logic of consequences could also explain why regulators at the provincial level, at furthest distance from the central government, may have less of an incentive to enforce regulations for quality monitoring. Due to distance and stretched resources, central regulators are not able to regularly keep checks and balances on implementation at the provincial level. Fewer accountability mechanisms for activities at the peripheral level mean that the consequences of not acting are low.

9.3.3 Policy developments in context

As demonstrated in the analytical framework for this study, the national and international contexts largely influence the framing processes around a policy problem, as well as the policy pathways proposed in response. At the national level, the political culture of a country, the degree of transparency and the structural arrangements for policy making, are important factors to consider when analysing the effect of frames on policy developments. The level of economic development and GDP also influences this process. For example, the regulatory frame was evoked on the common understanding that NRAs with small public health budgets across the three countries, lack the necessary resources to enforce the existing rules and regulations and to hire or train human resources to implement drug regulations fully. Both Cambodia and Laos have lower GDPs and smaller health expenditures than Thailand. Thailand, on the other hand, boasts a more developed domestic pharmaceutical industry. This factor could explain the politically-driven priority towards the protection of the pharmaceutical industry.

The importance of structural arrangements in the implementation of rules of regulations also seemed relevant. Ineffective decentralization of the health system, in terms of the delegation of roles and responsibilities to provincial health offices and inefficient reporting system to central levels, results in an ineffective implementation of drug regulations in peripheral areas located furthest from the central government. Structural differences in health systems and health financing across the three countries influence the focus on either capacity or capability building. Laos has a comparatively less robust health system in general and it might be for this reason that respondents emphasised the need for wider health systems strengthening (HSS), aimed to improve access to health services in general. Government level respondents pointed to a lack of technical expertise for drug quality testing. In comparison, Thailand is faced with different issues linked to its status as a higher-income economy with better access to the internet, making e-pharmacies a new source of contention. By invoking the regulatory frame, respondents in Thailand explained that current measures to monitor the circulation of poor-quality medicines are not commensurate with the structural reality of the pharmaceutical market, where many poor-quality products including food supplements and medicines are being sold online.

The political culture in each country, as well as the inclusivity of the policy formulation process through policy communities and cross-sectoral consultations, also seem to influence policy developments. The degree of systematic cooperation and communication between the NRAs and customs and police officials, for example, impacts the success of inspection efforts.

The results suggest that proposed policy solutions are largely influenced by both the political stream (political culture and governance structures), as well as the problem stream (i.e., the framings) (Kingdon 1984). As part of the political stream, issues related to political will are also important to put into context. An expert respondent explained that some of the leaders in charge of drug regulation or the health system perceived the problem of poor-quality medicines as a problem of the poor and did not necessarily feel directly affected by it, as they seek treatment in capital cities where there is a greater guarantee of quality of service and health products (EXP17_INGO20150716). This could explain the low political priority granted to the wider issue of poor-quality medicines.

Adding to this complex reality, patients and consumers are not always fully aware of the problem of poor-quality medicines and therefore are not in a position of knowledge to hold the government accountable. There is more awareness and political pressure in terms of the target of malaria elimination, however. I argue that the goal of malaria elimination could instead form the motivation and commitment of leaders to focus efforts on improving access to affordable ACTs and to reduce the circulation of oAMTs. Beyond the challenge of maintaining political momentum towards malaria elimination in border areas, where malaria is still present, the context does not seem to favour strong political will towards addressing the circulation of falsified medicines in these areas. These results provide valuable insights on what might motivate political will to dedicate time and resources towards the problem of poor-quality medicines.

Despite a certain degree of openness among government respondents in admitting to the lack of data transparency or the weakness of the enforcement system, it was apparent, from my experience in conducting this study, that the problem of poor quality medicines remains a very politically-charged issue across the three countries. The political sensitivity is especially apparent in settings where mechanisms for accountability for enforcing drug regulations are limited. This allows policy actors to shift responsibility away. Results demonstrate that gaps in the governance of drug regulatory affairs remain, including vulnerabilities to corruption of drug regulators. This may affect compliance across regulatory functions (Mackey & Liang 2012). Reports by the GF Office of the Inspector General in 2013 and in 2017 on Cambodia, shed light on some of these issues, pointing to allegations of fraud in rounds one through nine of GF funding for malaria. As a result, the Principal Recipient status was transferred from the national malaria centre (CNM) to UNOPS. A dispute over the disbursement of GF funds still lingers in Cambodia, since the GF tried to tighten control on the expenses for travel and accommodation of the CNM. Because of this dispute, Village Malaria Workers have not been

paid to continue with their malaria surveillance efforts, which may impede access to quality AMLs for remote and at-risk populations and foster the illegal underground sale of AMLs in border areas. It is interesting to note that sanctions against officials who are involved in the circulation of such products have reduced in recent years. These context-specific political challenges may persist unless more robust mechanisms of increased accountability are put in place.

At the international level, cross border situational elements such as the reinforced economic integration process of the ASEAN Economic Community are also said to influence the salience of frames among policy actors and guide policy decisions. A dominant international factor common to all three case countries was the flow of MMPs, and the perceived contribution of this flow to the circulation of poor-quality AMLs. This was reported in Thailand with regards to migrant workers in border areas with Cambodia and Myanmar. Historically, Thailand has had to deal with complex criminal networks of narcotics triggering the formulation of tough penalties against illicit drug traffickers. This might explain law enforcement officials' propensity to focus on the narcotics trade rather than the circulation of poor-quality medicines. In Laos, the threat of smuggling was particularly present in respondents' accounts because of the country's long borders and its position as a transit country of the Mekong. Another international factor articulated in different ways among Thai and Lao respondents, was that of regional investments and the inequality that these investments perpetuate in the region. The establishment of the AEC by 2015 might have facilitated the securitisation of the issue of poor-quality medicines due to the heightened risk of smuggling through increasingly porous borders. It would be interesting in future research to explore the impact of the AEC on the policy issue of poor-quality medicines.

9.3.4   Access to quality medicines: a secondary policy goal

Different articulations of a frame can lead to similar policy outcomes. Despite variations in how the problem of poor-quality was framed in Cambodia, Laos and Thailand, the problem is rarely equated with international crime across the three countries. Despite efforts to revise legal provisions and penalties against the production, sale and distribution of falsified and substandard medicines, there is limited involvement of the judiciary and law enforcement organizations, who are crucial partners in efforts against this threat in the three countries. Instead, government officials emphasised the importance of drug safety and efforts against substandard medicines, in response to the threat of drug resistant malaria. Despite the securitisation of the problem of poor-quality medicines, results suggest that there has been a

limited focus on post-marketing surveillance and in regulating against falsified medicines specifically.

My analysis of policy developments in Cambodia, Laos and Thailand suggest a process of frame competition between the security frame, the health systems frame and the regulatory frame. Policy decisions are motivated first and foremost by the goal of reducing the circulation of oAMTs, strengthening efforts against substandard and unregistered AMLs and therefore supporting malaria elimination efforts. My observation is that the goal of improving access to quality antimalarial medicines becomes a secondary goal under the overarching aim of eliminating malaria. Evidence of artemisinin resistance as a threat to malaria elimination aligns the issues evoked under both the medical (artemisinin resistance and drug efficacy) and the security frame (the threat to national security). Through this alignment of actor priorities, the policy choices are aimed at protecting the state against a deadly infectious disease, as reflected in analyses of policy processes. Regulatory frameworks on the management of pharmaceuticals beyond AML commodities primarily focus on the availability and accessibility to affordable essential medicines, without directly targeting the circulation of falsified medicines. There are limited policy efforts beyond drug safety and to address the crime of medicine falsification, or the circulation of poor-quality AMLs in the informal supply chain. Based on the results of this study, I would argue that the adoption of the ATM policy goal would need to be reflected in revised regulatory frameworks that provide stronger provisions and accountability mechanisms for the enforcement of post-marketing surveillance activities for all categories of medicines. A clear observation, however, is that malaria elimination and the focus on monitoring the quality of antimalarial medicines remains a relevant entry point on which to engage regulators on the problem of poor-quality medicines.

9.4   A coordinated regional policy response

Despite some similar policy outcomes, results show that the policy problem of poor-quality medicines is perceived differently in Cambodia, Laos and Thailand. This explains the variations in policy developments to monitor the quality of medicines. There is a need to reconcile variations in policy outcomes and to overcome the political sensitivity for a more coordinated policy response to what is a trans-national health challenge. While strengthening drug regulatory systems and improving quality monitoring activities to reduce the circulation of poor-quality medicines is the responsibility of national governments, respondents recognise the gains to collective action. A coordinated and cross-sectoral policy response is required in order to address all dimensions of this complex policy problem – its social, economic, political and legal dimensions. A coordinated cross-border response also triggers a sense of shared

responsibility towards the cross-border circulation of poor-quality health products, and avoids shaming individual countries as the source of the problem. The gains towards collective action and more integration may drive political will for more joint action, and encourage countries to commit resources towards active quality monitoring of pharmaceuticals without the weight of blame.

The uneven regulatory capacity and capability between Cambodia, Laos and Thailand means that countries could benefit from the standardisation of processes for the regulation of pharmaceuticals and to promote the exchange of expertise. Promoting regulatory convergence could help countries strive towards being equally equipped to monitor the quality of medicines. This is not without difficulties, however, because of the context-specific challenges across the GMS. For example, the development gap between member states in the GMS means that processes of integration are slow and laborious, with each member state working to a different timeline according to its level of readiness. Other challenges arise from the nature of policy-making in Southeast Asia and between ASEAN nations. The ASEAN decision-making process sometimes referred to as the 'ASEAN Way' (Goh 2002; Acharya 1997) is defined by the primacy of national sovereignty, the prevalence of national interests over the common good, and the culture of rule by consensus (Lamy & Phua 2012; Acharya 2009; Acharya 1995). No legally-binding decision is taken unless it is unanimously endorsed by all ten member states. The ASEAN does not provide an ideal platform therefore to foster coordination on politically sensitive issues. The limitations of the ASEAN Way[57], and context specific challenges to regional cooperation, mean that regional integration beyond the economic and trade realm is sparse. Previous efforts towards integration among ASEAN members have been centred on the promotion of trade and economic growth, with a comparatively limited emphasis on the socio-cultural community pillar of the ASEAN Blueprint under which health falls. My analysis of the results suggests that mobilising a *regional* health security frame could reconcile cross-border efforts to strengthen health systems and to generate the political will needed to address bottlenecks in the drug regulatory space.

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[57] The ASEAN, as a diplomatic platform and a respected regional organization, has the potential to support stronger regional cooperation and concerted action against health threats by convening senior level policy makers. Regional coordination through the ASEAN relies predominantly on the formulation of non-binding measures in the form of declarations. The extent to which these declarations trigger policy change at the national level is questionable. The principle of non-interference, at the source of Southeast Asian politics, means that ASEAN nations retain the right to adopt or to reject any guidelines from ASEAN. The shortage of funds is another recurrent obstacle to ASEAN regional cooperation.

9.4.1.1   Health security concept in Southeast Asia

Based on the results of this study, it appears that invoking the health security frame may further align policy actors' priorities towards the ATM goal. The concept of health security as will be demonstrated in this section, is not alien to the GMS or even to Southeast East Asia. In fact, the ASEAN was first created in 1967 as a 'security community' (Acharya 1995) in response to regional instability. ASEAN member states have operated within a traditional construct of security which has gradually evolved to incorporate non-traditional sources of security, including health threats (Caballero-Anthony *et al.* 2006; Emmers 2004; Hyun *et al.* 2000). The focus of non-traditional security among ASEAN nations is on coordinated efforts to combat narcotics trafficking or other activities related to smuggling of illegal products. Such conceptions of non-traditional security are an 'expression of Asian regionalism' (Arase 2010). Historically, challenges linked to the cross-border movement of people have also been high on the agenda. ASEAN member states have engaged in regional initiatives against transnational crime since the 1970s. Endorsed in 1997, the ASEAN Declaration on Transnational Crime underscores the threat of transnational criminal activity for the regional stability (Emmers 2003). To support regional coordination against transnational crime, several institutional mechanisms and action plans have been developed, such as the ASEAN Ministerial Meeting on Transnational Crime (AMMTC) or the ASEAN Plan of Action to Combat Transnational Crime. ASEAN nations have also developed a coordinated response to natural disasters, with Cyclone Nargis in Myanmar in 2008 acting as a trigger of such efforts, leading to the development of regional disaster preparedness plans. Issues of non-traditional security in relation to transnational crime or disaster response extend beyond the traditional definition of security. Nevertheless, the ASEAN focus on non-traditional security threats are motivated first and foremost by the preservation of national economic interests and regional stability and prosperity.

Following the 2003 Severe Acute Respiratory Syndrome (SARS) epidemic, infectious disease threats have been considered as regional non-traditional security challenges that transcend borders, endanger Asian economies and require a coordinated response (Labonté & Gagnon 2010; Caballero-Anthony 2008; Caballero-Anthony *et al.* 2006; Emmers 2007). Global health issues have gained recognition as non-traditional security threats mainly because of the risks these pose to economic development. This was again true of the Avian Influenza A (H5N1) in 2005 and Influenza Pandemic (H1N1) in 2009. Mechanisms implemented at the ASEAN level in response to regional health threats as a result are focused on a coordinated response to emerging infectious diseases as immediate threats to populations. Such mechanisms include

the Highly Pathogenic Avian Influenza (HPAI) Task Force (2004) and the ASEAN Plus Three Emerging Infectious Disease Programme (2004). The ASEAN Socio-Cultural Community Blueprint in 2009 and the ASEAN Strategic Framework on Health Development (2010- 2015) represent milestones for Southeast Asian regional cooperation in health. The Blueprint and Framework propose a multi-sectoral and multi-stakeholder approach for building disaster-resilient nations and safer communities and ensuring a drug-free ASEAN, but also encourage wider capability building for communicable disease control, providing access to healthcare and promoting healthy lifestyles. More recent global health threats such as the Ebola Viral Disease (Ebola), the Zika Virus and the Middle Eastern Respiratory Syndrome (MERS), have triggered renewed interest in the promotion of regional coordination to maximise efficient use of resources and expertise across borders and to improve the surveillance and response towards emerging health threats. Despite this momentum, ASEAN cooperation in health systems strengthening remains limited. While recent global epidemics have led Southeast Asian leaders to the realisation that health threats can have cross-border implications and require coherent and coordinated policy response, regional coordination remains largely state-centric.

ASEAN efforts to improve access to quality medicines have been modest to date and largely limited to training and information sharing activities, such as through the underutilised ASEAN post-marketing alert system (PMAS), established to notify national regulatory agencies in the region about unsafe or defective health products (Nwokike *et al.* 2013). Regardless, the issue of counterfeit or falsified medicines has been part of recent institutional dialogues in the region. The first action plan to Implement the Joint Declaration on ASEAN-China Strategic Partnership for Peace and Prosperity included a specific commitment to 'strengthen cooperation to prevent production and spread of counterfeit drugs' (ASEAN 2004). Additionally, the ASEAN-China Conference on Combating Counterfeit Medical Products was held in Jakarta in 2007. It is reasonable to expect that further collaborations could follow (Lamy & Liverani 2015). Under the ASEAN Plus Three arrangements, stronger collaboration with China would be crucial, given that this country has been a source of substandard medicines in the Mekong region (Newton *et al.* 2008). To date, however, ASEAN collaborations with China on transnational crimes have mainly focused on narcotics. Regional coordination on the illegal circulation of falsified medicines is further hampered by political tensions between ASEAN nations of the Mekong. While the establishment of the ASEAN in 1967 has contributed to the promotion of peace and peaceful resolution of conflicts, land border disputes are still a serious challenge to political stability in the Mekong region (Amer & Thao 2009). Recent tensions between Cambodia and Thailand over the sovereignty of the area around the Preah Vihear temple are just one example. Such tense conflicts may indeed

negatively impact efforts towards cross-border inspections, or to track the movement of suspicious pharmaceuticals across borders.

The ASEAN way and the focus on the preservation of national and economic interest when addressing health issues, suggests limited opportunities for a coordinated response to strengthening health systems and drug regulatory for access to better quality medicines. Taking these limitations into consideration, the primacy of national sovereignty and context specific challenges, I argue that invoking the regional health security frame may trigger a sense of shared responsibility and promote policy coherence. Alternatively, introducing mechanisms to share best regulatory practices in each country setting may help promote more sustainable cross-sectoral collaboration and strengthen national health systems without impeding national sovereignty.

9.4.2   Invoking the regional health security frame

The national security frame seems to resonate in the countries studied, as it is in line with the ASEAN principles of non-interference and preservation of sovereignty. The understanding of health security in Southeast Asia is predominantly 'state-centric', revolving first and foremost on the preservation of national interests and the welfare of national populations. This was apparent in the framing of the problem of poor-quality medicines as a *national* security issue. As explained by Rushton & Youde (2015), the securitisation of public health issues in the interest of national sovereignty preservation, could have negative implications for cross-border cooperation. The securitisation of global health issues as national threats can lead to distortion of the global health agenda. In the case of poor-quality medicines, the risk of securitisation is an emphasis on protectionism rather than cooperation. For this reason, framing the threat of poor-quality medicines as a *regional* health security threat might encourage shared responsibility and foster regional cooperation. The region health security frame brings the issue of poor-quality medicines into the realm of health, economics and foreign policy, and could help raise the issue on the regional political agenda.

The concept of non-traditional security is essentially based on an inter-subjective understanding of a policy issue (Lee & Chan 2007). For this reason, ideas play a role in shaping both processes of securitisation and of Southeast Asia integration (Acharya 2009). The concept of regional health security has been brought forward recently by leaders in Southeast Asia. This was the case at the East Asia Summit (EAS) in November 2015 for example, where 16 Heads of State issued a statement committing to enhancing regional health security in response to infectious diseases with epidemic and pandemic potential (East Asia Summit 2015).

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Additionally, the post-2015 ASEAN Health Development Agenda calls for more resilient and robust health systems in response to communicable and infectious disease threats. This reflects the WHO 2005 International Health Regulation (IHR), a global instrument that provides normative guidance for inter-governmental cooperation against the global spread of infectious diseases (Kamradt-Scott 2015). The concept of regional health security is predominantly centred around the threat of emerging infectious diseases. Nevertheless, framing the issue of poor-quality medicines as a regional health security concern and a threat to infectious disease control in the region, could not only prompt national policy choices to dedicate further resources to the ATM goal, but it may also elevate the issue beyond national security to encourage regional coordination.

9.4.2.1 Human security and regional social integration

The challenge to invoking the regional health security frame around the problem of poor-quality medicines, is that the official definitions of falsified and substandard medicines are not consistent across countries. There is a need for a common definition of poor-quality medicines among ASEAN states that encompasses all dimensions of this complex issue. What is required is a shift in how the problem of poor-quality medicines is understood – as a threat to both the economic and social integration of the region. One way to do so could be to link the concepts of regional health security and human security – advocating for the need to address the problem of poor-quality medicines to protect populations across Southeast Asia.

> Health and human security could also converge through regional approaches, which can provide a middle path by recognizing the interdependencies of systems involved in addressing health risks, vulnerabilities, and threats. (Caballero-Anthony & Amul 2015, n.e-book)

The concept of human security first emerged in the ASEAN Plus Three framework in 2001 regarding environmental protection (Caballero-Anthony & Amul 2015; Evans 2004). Human security is also encompassed as a feature of the ASEAN Healthy Lives for a Healthy Community objective. The concept resonates with member states' desire to protect populations. In fact, human security could be included within the concept of traditional security (Hyun et al. 2000), as an essential component of protection of a nation's population. The human security concept promotes a human-centred approach to security issues that goes beyond the state-centric focus on the protection of material or economic interests (Caballero-Anthony & Amul 2015; Caballero-Anthony 2008; Ogata & Sen 2003). This aligns with the accounts of government level respondents on the protection of national interests including of

populations. Government level respondents across the three countries acknowledged the challenge of eliminating malaria among MMPs and hard-to-reach communities due to poor access to quality AMLs. Promoting a human-centred approach to health security to address the challenge of hard-to-reach and at-risk communities, may therefore resonate well with regulators in this field. It could promote awareness of the problem of MMPs as a shared responsibility and encourage coordination of efforts to address this challenge jointly.

9.4.2.2   Health systems strengthening as a long-term approach

Linked to the human security concept, the regional health security frame could advocate for broader health systems strengthening and encourage regional coordination beyond the response to emerging infectious disease. As the results demonstrate, respondents note the need to strengthen health systems and regulatory capacity for surveillance to ensure access to quality medicines. Advocating for a health systems strengthening approach to address regional health security threats may be one way to promote the ATM goal, harness political commitment and push for regulatory convergence. Strengthening health systems to support health service delivery directly promotes access to health and to health products for all. This approach may resonate well with leaders in Southeast Asia and the Mekong, as it could be perceived as contributing to the reduction of poverty in the region and would contribute to the socio-cultural integration of ASEAN states. Health systems strengthening would also contribute to the reduction of social inequalities and support more even economic development, as more robust health systems across the region would make it easier for countries to protect themselves against emerging and re-emerging health threats.

Health security may be perceived as a 'global public good' (Caballero-Anthony *et al.* 2006, p.111), and health security threats as communal challenges that engage the responsibility of not just states, but also non-state actors. Leveraging the regional rather than the global health security frame has more chances of instigating change, as noted by Caballero-Anthony & Amul (2015). Regional health threats are based on the same risks and challenges and vulnerabilities, and a security construct is inevitably built on common contextual factors. A regional approach to health security is more likely to resonate with policy makers and to encourage policy change, as it would take into account the challenges specific to Southeast Asia.

> Ideally, regional approaches to health security would not be so global that they
> skew the focus towards pandemics, nor so local that they neglect the potential
> spill over and transfer of the burden of health insecurities to those already

vulnerable. They would also be more able to address context-specific conditions so as to reach the poor and vulnerable members of populations most likely to be affected by disease. (Caballero-Anthony & Amul 2015, n.e-book)

Nevertheless, as the results demonstrate, Southeast Asian member states are faced with different challenges. In view of the varying nature of their regulatory processes, political cultures and level of resources, tailoring responses to each country might be more suitable. This could occur through sharing best practices and adapting mechanisms that respond to the needs and gaps of each regulatory system. This may in turn encourage greater policy coherence and facilitate access to quality assured essential medicines across the region.

9.4.3 Promoting policy coherence

Health systems strengthening in response to regional security threats and to improve access to good quality medicines can be facilitated at the regional level by promoting policy coherence through the transfer of policies. This might in turn encourage greater convergence between drug regulatory systems. The economic disparities and gaps in development across ASEAN member states represent a challenge to equitable integration (Speers *et al.* 2016). Currently, less-resourced member states (particularly Cambodia, Myanmar, Lao PDR and Vietnam) need support to benefit from the ASEAN integration process. This is particularly relevant considering the changing landscape of regional investments in Southeast Asia and the resulting sense of uneasiness among poorer ASEAN nations.

The increased connectivity between GMS countries and other Southeast Asian nations brings both opportunities and challenges. The increased trade and more porous borders between nations also heightens risks of smuggling and the rapid spread of diseases across borders. Large numbers of unregistered products routinely flow through the porous GMS borders, and yet we have little information on the channels through which poor-quality medicines flow into and out of countries. Policy coordination between countries on surveillance, detection, quality control and systematic sharing of information could therefore be useful to address such trans-border challenges.

9.4.3.1   Policy transfer and information sharing

Policy transfer between GMS countries, including the exchange of information and policy best practices around drug regulation, may be one way to foster a more coordinated policy response against falsified and substandard medicines. Policy transfer is the adoption or application of a strategy, policy, programme, plan or a tool from one policy context to another because of its

perceived feasibility, validity and adaptability (Bissell *et al.* 2011; Dolowitz & Marsh 2000). The transfer of knowledge and expertise between regulators, members of the ministries of health and law enforcement officials, for example, offers the opportunity for alignment of policy responses across border in response to the cross-border challenge of poor-quality medicines. It also leads to a more efficient use of limited financial and human resources by drawing on lessons learned from neighbouring countries. Countries are left with the decision to adopt or reject specific policies, and so this approach is less likely to be perceived as impeding on their sovereignty. Sharing best practices between countries may also facilitate the scaling up and optimal use of existing mechanisms in place to target efforts against the circulation of falsified or substandard. It can facilitate coordination of activities between cities or provinces on two sides of a border. This is especially relevant in a context where borders remain highly porous.

The first opportunity for alignment that would benefit a coordinated policy response, is the delineation of a shared definition of substandard and falsified medicines at the regional level. A common definition could facilitate more coherent policy responses to address both drug safety and security. Another opportunity may be to improve **i**nformation sharing to support investigation of cases of poor-quality medicines. Mechanisms for information sharing can facilitate a more transparent and efficient coordination of efforts across borders. Information on drug stock seizures between customs official at border areas, for example, could support efforts to map the illicit trade routes of falsified or substandard health products. The currently limited data available on the circulation of poor-quality medicines makes it more challenging to convince policy makers to dedicate resources to prevent their circulation. As Philippe Guérin notes: 'if you cannot quantify the problem, you do not have the problem' (Guérin 2015). Integrated surveillance systems and increased information sharing on poor-quality medicines may raise awareness about the scale of the problem and better guide future policy decisions. It seems like a relevant starting point that can better guide policy decisions and harness political will.

On improving access to quality AMLs, respondents in this study highlighted the success of some key policy mechanisms showing potential for scale up. The Village and Mobile Malaria Workers, for example, actively support case detection, reporting and distribution of quality AMLs. The malaria posts in border areas of Mekong countries undertaking this work could also collect information on adverse drug reactions to substandard treatments, and report on the whereabouts and the nature of unlicensed and itinerant points of sale for AMLs. The Public-Private Mix (PPM) programs in Cambodia and Laos also facilitate the diagnosis and reporting

of malaria cases and the distribution of quality assured ACTs through the private sector pharmacy outlets. While the PPM initiatives are managed by different institutions in each country, respondents noted the success of the program in improving access to quality AMLs by integrating private sector in the distribution chain for AMLs. Scaling up this program to other provinces or to neighbouring countries and involving the private sector for health service delivery into the malaria program, could help reduce the demand for AMLs outside of the formal distribution chain. As a third example, the sentinel sites under the USP's Promoting the Quality of Medicines program, currently supports NRAs' efforts to sample and control the quality of AMLs. These are efficient existing mechanisms that can be scaled up across provinces, provided the necessary financial and human resources are mobilised to do so.

9.4.3.2   Regional regulatory convergence

Aligning regulatory processes for better coordination between NRAs, could overcome shortfalls in regulatory capacity to ensure even oversight of medicine quality across borders. Regulatory convergence[58] involves streamlining activities around the pre-market approval and post-market surveillance of health products, allowing for more efficient regulatory systems. Encouraging reliance[59] between NRAs can not only improve efficiency, but can also support the integration process of ASEAN by reducing gaps between regulatory institutions. This is particularly relevant to ensure that all ASEAN member states benefit equally from the reduction of barriers to trade. Promoting regulatory convergence could ensure that the reduction of trade barriers and the potential increasing flow of illicit products across borders, are met with improved regulatory convergence for joint efforts to monitor the circulation of poor-quality medicines. Regulatory convergence directly contributes to health systems strengthening by improving access to priority and quality assured medicines for all. Beyond trade integration, it could also improve access to quality essential medicines for all, by facilitating the expedited approval and roll out of quality-assured medicines.

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[58] While regulatory harmonisation is the promotion of uniform guidelines, regulatory convergence is a procedure whereby processes become more similar rather than uniform, through the gradual adoption of common guidelines and standards. Regulatory convergence allows nation states to retain a certain degree of sovereignty over the regulatory process. Nation states are still responsible for drafting and reviewing national laws and policies for the regulation of health products (United States Food and Drug Administration 2017).

[59] Reliance between NRAs occurs when better resourced NRAs share product reviews and assessments with other, less endowed NRAs. The latter accept the results of these reviews and use this information for their own regulatory processes from market authorisation to pre-market quality controls. This can save considerable costs for less-resourced and ill-equipped NRAs.

The ASEAN Pharmaceutical Product Working Group (PPWG), set up in the 1990s, works to standardise technical procedures and quality requirements for the registration of pharmaceutical products, through the ASEAN Common Technical Dossier (ACTD) to support the trade in pharmaceutical goods under the ASEAN Free Trade Agreement. Standardising technical regulations is perceived as valuable in that it supports both the pharmaceutical sector and economic integration (Pettman 2013). The PPWG is an important mechanism to encourage reliance between national regulatory authorities and to reduce delays in the registration of new AMLs for treating artemisinin-resistant strains of malaria. The extent to which activities of the ASEAN PPWG have been successful is questionable, however. While several ASEAN member states have pledged to use the ACTD in their registration processes, this rarely occurs in practice with individual countries still requiring a different set of information to grant a product market approval. Furthermore, regional regulatory convergence thus far has been primarily focused on pre-market activities and the registration of new medicines, rather than on post-marketing surveillance and quality monitoring. Post-market activities could benefit from further regulatory convergence. Laboratory testing capacity for AMLs is a challenge in Cambodia and Laos, where national laboratories are not adequately equipped or staffed for the task. Better-resourced countries, like Thailand, could provide technical support to other laboratories in the region to set up Standard Operating Procedures and work towards WHO-pre-qualification status. Networks to encourage the sharing of expertise between laboratories, including the NOMCOL facilitated by the USP, could be scaled up. University networks, such as Chualongkorn University in Thailand, may also support laboratory capacity building in the region through training programs. Information sharing mechanisms could also support regulatory convergence, for example if Thailand actively shared the Thai pharmacopeia with neighbouring countries. Such activities would contribute to regulatory and health systems strengthening.

Regulatory convergence may only be possible if it is promoted progressively and responds gradually to priority regulatory gaps in each country. However, the ASEAN PPWG may not be the optimal platform through which regulatory convergence can be encouraged. Various international development partners operate in this space to promote stronger regulatory processes and have provided capacity building support to individual countries. NRAs should retain ownership of this process and request technical capacity building assistance as and when necessary. Capacity building support and sharing of best practices need to address specific context challenges and should also be tailored to country specific needs – i.e., encourage cross-sectoral collaboration between government agencies.

9.5 Reflections on the global health problem of poor-quality medicines

This section reflects on the implications of the results of this study on the global health policy issue of poor-quality medicines. The goal of ATM was first addressed at the global level as detailed in Chapter 2. As the literature reports, there is no adequate global framework to guide action against poor-quality medicines (Mackey 2013). Global health institutions thus far have predominantly focused on the prevention, surveillance and response to emerging and re-emerging infectious diseases that pose a more direct threat to both low and high-income countries, with access to quality assured medicines only as a tangential objective. Historically, the priority of these institutions has been to preserve the interests of higher income countries (Ooms & Hammonds 2016). Specific mechanisms to guide national efforts against poor-quality medicines, such as the Medicrime Convention (Council of Europe 2011), propose a model law that is largely ill-adapted to respond to the complex challenge of both substandard and falsified medicines. The Medicrime convention which only recently entered into force (January 2016), aims to guide the formulation of rules and regulations at the national level, binding as the first 'international standard for criminalising the manufacture and distribution of counterfeited medicine' (The Lancet Editorial 2012). Regardless, the recommendations held within this convention centres first and foremost on the protection of patent rights as it refers to 'counterfeit medicines' (Attaran *et al.* 2011). The Medicrime Convention fails to qualify the falsification of medicines as a crime (Attaran *et al.* 2011). Authors on the problem of poor-quality medicines argue that there is a gap in the global health governance[60] space to address the challenge: 'A formalized and multi-stakeholder governance mechanism is needed to address the issue' (Mackey 2013), its economic, socio-cultural, legal, and political determinants. Here I reflect on various approaches for both state and non-state actors to influence the policy response to poor-quality medicines and to sustain political will and commitment for the ATM goal.

9.5.1 Regional health governance framework against poor-quality medicines

My observations while analysing the data from this study, suggest that promoting a regional, coordinated response to the global health problem of poor-quality medicines, portrayed as a regional health security concern, may promote political commitment. Since global governance approaches have been sporadic and ill adapted to sustaining such a commitment to the ATM goal thus far, a regional approach may be more successful in doing so. A regional approach

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[60] Global health governance (GHG) can be defined as a framework for policy leadership to address cross-border health policy problems exacerbated by globalisation (Lee *et al.* 2002).

may have the benefit of feeling 'closer to home' and promoting a policy goal that is more relatable to leaders facing common challenges. Roggeband *et al.* (2014) argue that the regional level offers another layer of cross-border discursive opportunity around an international norm or policy goal. My argument would be that a regional forum for policy coordination bridges the gap between global and national level efforts. This regional governance agenda can be supported by several policy actors, that can contribute efforts to address all determinants and challenges of the problem of poor-quality medicines – from the socio-economic to the political and regulatory constraints.

Results demonstrate that policy processes at the national level are more responsive when the problem of poor-quality medicines is coupled with an agenda to fight emerging and re-emerging infectious diseases, in this case artemisinin-resistant malaria. One strategy to trigger political commitment could be to frame the problem as a challenge to the control and elimination of infectious diseases in the region. Malaria elimination offers a useful entry point to engage leaders on the problem of poor-quality medicines. A starting point to a regional health governance response would be the convergence of legal definitions of substandard and falsified medicines in order to promote a two-pronged policy response. One response, under the realm of drug security, could encourage engaging law enforcement officials and ministries of trade, justice and defence. Policy efforts to reduce the circulation of substandard medicines could focus on improving drug safety and strengthening drug regulatory systems. Both parallel approaches may contribute to wider health systems strengthening against shared health threats in the region.

The other narrative that seems to resonate among policy actors is the health systems strengthening narrative. This suggests promoting the ATM alongside broader efforts to promote access to health services and health products for all, and advancing the right to health might trigger political commitment (Hammonds & Ooms 2014). This approach is more likely to be successful if it is inserted within a broader regional health governance framework. As Caballero-Anthony & Amul (2015) point out, there are tensions between a state-centred and a human-centred response to a health security issue. In the case of poor-quality medicines, the former tends towards infectious disease control and elimination for national security, while the latter brings in the health systems strengthening perspective. The tension between these two approaches could be reconciled with the leadership of non-state regional actors and through mechanisms that engage the responsibility of leaders towards health systems strengthening for regional health security. High-level forums (such as the ASEAN Ministers Meetings) where leaders agree on high-level political priorities and targets determining the allocation of

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resources, could drive political commitment towards the issue of falsified and substandard medicines[61]. As expressed earlier in this chapter, however, efforts to strengthen health systems need to address context specific challenge and respond to the priority needs of countries individually, as there is no one size fits all approach to regulatory capacity building

9.5.1.1 Mechanisms for accountability

The current regional health governance framework requires stronger accountability mechanisms for sustained political commitment and to engage the responsibility of governments to jointly advance the regional health security agenda. As discussed in section 9.4, increased opportunities for policy transfer and regulatory convergence might help to increase political commitment and to engage government accountability by facilitating joint action. The ASEAN post-2015 Health Development Agenda (ASEAN 2015) proposes mechanisms for improving accountability and using evidence-based approaches to set health priorities and measurable targets, with a commitment to implementation across sectors. Other mechanisms to increase accountability and to track process could mirror the ASEAN Economic Community Scorecard, which was designed to chart progress towards economic integration in Southeast Asia. Issues such as access to medicines and access to health that are broader in scope are difficult to retain on the political agenda (Caballero-Anthony & Amul 2015), but mechanisms to track progress and keep leaders accountable could help sustain this political commitment. Expert respondents noted that increased checks and balances through regional coordination could not only maintain political will, but also increase the transparency of implementation processes and limit instances of corruption with regards to the circulation of poor-quality medicines (EXP17_INGO20150716).

9.5.2   Network of actors for regional health security

A framework for health governance at the regional level could provide some of the needed checks and balances. At the same time, a regional framework for health governance could better leverage the resources and capacities of policy actors and non-state partner organisations in the drug regulatory space for the integration of drug regulatory efforts in Southeast Asia. These networks of state and non-state actors could also ensure that capacity building activities are tailored and adapted to each country's needs and priorities. Global health is a dynamic

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[61] At the 2014 of ASEAN Health Ministers Meeting held in Vietnam, for example, leaders stressed the need for ASEAN members to strengthen health systems and reinforced the need for 'Better Health for the ASEAN Community Beyond 2015' (ASEAN 2014). They also expressed concern at the rising incidence of infectious diseases, including the Ebola Virus Disease, and the negative impact on the socio-economic development of the region (ASEAN 2014).

space for global governance (Youde 2012), through which agencies can engage with a plethora of actors – from global health institutions and international donor organizations to technical agencies and civil society organizations (CSOs). In this regard, non-state actors such as CSOs and donor organisations could provide stronger mechanisms to hold governments accountable to a common agenda for policy change. The mobilisation of a regional health security frame around the problem of poor-quality medicines could also leverage the resources and expertise of a multitude of partners in this 'action arena'[62], from CSOs at community level, to non-governmental global health institutions. My observation from this thesis is that non-state policy actors form a strong network that can support the integration of efforts for malaria elimination, as an entry point into a wider objective for health systems strengthening.

9.5.2.1   Inter-governmental organisations

Various organisations have been mentioned in this study as promoters of the ATM goal. The WHO, as an inter-governmental organisation, has the authority to elaborate and promulgate laws (such as the IHR institutionalising the right to health) and is perceived as a having the normative power to guide governments' policy reforms and decisions to improve access to quality medicines or to strengthen regulatory systems. As an example of its normative influence in the global health arena, the WHO promulgated the Framework Convention for Tobacco Control (FCTC), which provides guidance for states to review their rules and regulations to reduce tobacco consumption. Some of the measures in the FCTC regulate against the smuggling of illegal tobacco substances as products harmful to health. These measures set a relevant precedent for similar regulation against other illegal harmful products – such as falsified and substandard medicines. Attaran *et al.* (2011) argue that a Model Law should be created under the auspice of the WHO as the sole institution with the mandate to promulgate international laws. At the national level, WHO country offices can support capacity building efforts through technical assistance. The opportunities for regional coordination by the WHO on the problem of poor-quality medicines in the GMS, are limited by the fact that member state countries are split member between the WHO South-East Asia Regional Office (Thailand) and the WHO Western Pacific Regional Offices (Cambodia and Lao PDR) – with limited coordination of agendas between the two offices. The WHO's Emergency Response to Artemisinin Resistance initiative (ERAR), for example, has had limited success with few positive outcomes over the three years of operation. Mackey (2013) argues that while the WHO has a role to play in raising normative awareness about the problem

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[62] 'Action Arena' is based on the definition by Ostrom and Aligica, who refer to the policy space where stakeholders with an interest in access to medicines comes together through meetings or common programs of action (Ostrom 2009; Aligica 2006).

of poor-quality medicines through research and analysis, other organizations like the United Nations Office for Drugs and Crime are better positioned to deal with the issue of falsified medicines. The WHO plays an important role, however, in driving the policy response for increased drug safety – through capacity building of regulatory systems and by setting standards and guidelines to facilitate regulatory convergence.

Another international organization that has provided in-country support in the fight against poor-quality medicines including AMLs is INTERPOL. The role of INTERPOL is particularly relevant to push for the coordination of law enforcement agencies against the circulation of falsified medicines and in support of the regional security agenda. In this regard, INTERPOL is an important player in pushing the drug security agenda forward. INTERPOL supports cross-border investigations and the regional operations clearly showcase the trans-border nature of trafficking routes. While INTERPOL has provided some training assistance to allow customs and police officials to conduct such operations more systemically, such training activities remain ad hoc and INTERPOL's activities do not directly promote sustainable and long-term commitment by law enforcement officials to the goal of ATM.

9.5.2.2   Technical agencies as implementing partners

Another observation from this study is that CSOs also have a role to play in shaping the regional and global debate around a policy goal of access to quality medicines, and in supporting the effective implementation of existing rules and regulations at the community level. There is a need to harness the expertise and resources of existing implementing partner organizations in this policy space, for greater regulatory convergence and to contribute to health systems strengthening through capacity building activities. As the results demonstrate, the USP and the PSI have largely supported the process of interest formation around the policy problem of poor-quality medicines. They have also been partners in the implementation of rules and regulations to address this problem for AMLs and in strengthening the capacity of NRAs to monitor the quality of medicines. Technical agencies, through capacity building activities for sustainable support, contribute to building ownership of these processes by national governments. The United National Office for Drugs and Crime, through its Container Control Program, has also provided valuable technical capacity building support (in cooperation with INTERPOL) to customs officials for the verification of incoming containers containing pharmaceuticals and spotting potential fraud in documentations.

There are limitations to relying exclusively on inter-governmental bodies and non-governmental technical partners for policy change and to strengthen health systems effectively. As suggested by respondents in this study, the current regional governance space for policy coordination on the quality of medicines is highly fragmented. Several technical agencies operate in this space, often leading to duplication of capacity building efforts and with inadequate processes to identify priority areas for regulatory support. The various information sharing platforms such as the ASEAN Post-Market Alert System (ASEAN PMAS) or the USP Build Regional Expertise in Medicines Regulation, Information Sharing, Joint Investigation and Enforcement Mechanism (BREME), remain largely under-used. Regulators expressed confusion as to which mechanism to report the identification for poor-quality medicines through. Another limitation relates to the sustainability of these initiatives to support regional health cooperation. International health partners and technical agencies' operation is dependent on the sustainability of external funding (Liverani *et al.* 2012). The lack of continuity in funding for existing initiatives means that some efforts are discontinued. Relying on external funding for building regulatory capacity means that efforts are not always integrated within national structures to ensure a sustainable health systems strengthening approach.

9.5.2.3   Donor commitments towards malaria elimination

Renewed funding commitment towards malaria elimination through, for example, the Regional Malaria and Other Communicable Disease Threats Trust Fund (RMTF) in December 2013 or the Regional Artemisinin Resistance Initiative (RAI) (to renewed at the end of 2017), encourages multi-country, cross-border and multi-sector responses to the disease including strengthening drug regulatory systems. This supports the argument that malaria elimination remains a strong entry point in the Mekong region for the promotion of the goal to improve access to quality medicines. The malaria elimination agenda horizon up to 2030 in the Asia Pacific Region (Asia Pacific Leaders Malaria Alliance 2015) includes drug regulatory and health systems strengthening as a priority. In this manner, efforts to strengthen the drug regulatory space for access to quality AMLs could eventually benefit other therapeutic drug categories. It is by harnessing the expertise and resources of all actors in this space that a strong regional health governance framework can support the coordination of responses to improve access to quality AMLs and other essential medicines in the region.

Conclusion

Concluding thoughts

As demonstrated in this study, interpretations of the policy problem of poor-quality medicines vary across national settings. This is due to varying conceptions of quality and the differences in terminology used to define poor-quality medicines across countries. It is important to bear in mind, however, that the definitions reviewed in this thesis are English translations of official documents originally written in Lao, Khmer and Thai. The translations may have distorted the original meaning of the terms used and described, which is one of the main limitations of my analysis.

The determinants and drivers of the policy issue of poor-quality medicines are also perceived differently across categories of respondents. This has led to different pathways of policy response and limited evidence of cross-sectoral or cross-border cooperation to improve ATM. Reconciling pathways of policy responses requires, first and foremost, a common regional definition of poor-quality medicines in policy and legal documents. To avoid confusion of terms, this definition would have to be clarified in a common language (such as English). The availability of English translations of documents on medicines regulation is important as it reflects governments' willingness to share information on regulatory frameworks and processes. It is also a necessary pre-requisite to achieve policy coherence across borders and cross-border cooperation.

While policy actors demonstrated heightened awareness of the problem of poor-quality medicines, many highlighted limitations derived from the lack of data on the prevalence of substandard or falsified medicines. Respondents showed a strong inclination to evidence-based policy making. For this reason, further evidence and information sharing through regular and systematic post-market sampling of medicines, could fuel political will and inform policy decisions towards a more pro-active approach to improving ATM. In view of the discontinuation of GMS-wide data collection projects on the distribution of AMLs through unlicensed outlets such as ACT Watch project (under PSI), it appears even more crucial for regulatory systems strengthening activities to prioritize systematic sampling procedures and data collection.

Results also demonstrate that political will towards the ATM goal may be best harnessed through the alignment of the ATM goal with the security paradigm. The security paradigm can be used to raise attention towards a policy issue and place it on the policy agenda (Labonté &

Gagnon 2010; Balzacq 2005). The problem of poor-quality medicines, portrayed as a shared responsibility to protect the wellbeing of populations across borders, raises the importance of medicine regulation onto the political agenda. Beyond addressing the specific gaps and needs of national regulatory systems, good governance is primordial. Regulatory systems strengthening, encompassed within wider health systems strengthening objectives, should address issues of transparency and the effective management of limited resources. Policy actors need to be held accountable across sectors and beyond border for delivering on these objectives. Framing the problem of poor-quality medicines as a regional health security concern, engages policy actors in a discussion on improving cross-border coordination and promoting policy coherence. For fear of lagging behind, this could encourage policy actors to dedicate the necessary resources for the effective enforcement of existing rules and regulations.

As part of high-level advocacy among policy makers, the economic benefit of investing in regulatory strengthening and greater convergence across the region, could also trigger political commitment. This case should be made clearer. Beyond mechanisms for guaranteeing drug safety, regulatory capacity should be enhanced and needs to be geared towards improving drug security as well as drug safety. This requires cooperation across sectors, from regulators to law enforcement officials. It also requires greater synergy with non-state actors, including the pharmaceutical industry (in part for its financial resources and expertise in track and tracing of their own products) and academia (with further operational research to advice policy developments, for example).

To improve regulatory capacity and streamline efforts towards the ATM goal, innovative approaches to scaling up existing initiatives and mechanisms are crucial. For example, platforms or committees for substandard and falsified medicines may facilitate coordination between different sectors of government. Other mechanisms to connect development partners, national agencies and the private sector (such as the PPM programs), may be helpful to support better health service delivery and access to quality health products. Such initiatives could be scaled up and introduced in new settings. Technology (although it poses a risk in the form of e-pharmacies) is yet another tool that could be used to support the ATM goal, by facilitating the reporting of evidence of substandard or falsified medicines from the national, regional to the global level (feeding into the WHO Rapid Alert System, for example). Authentication and serialisation of quality-assured products is another way to harness technology for ATM, but may be too costly at this stage. In the meantime, introducing tools to empower consumers also has a role; the SMS for Life program for patients to verify the quality of AMLs by text

messaging (a project piloted in Tanzania) is one such example. Informing the public of their right to receive safe medicines and of the dangers of purchasing medicines through unlicensed outlets, should form an essential component of advocacy campaigns.

Contribution of this study

The findings from this study are useful to inform the future development of effective interventions at the national and regional level, to prevent the illicit trade of poor-quality medicines and to promote access to quality medicines in the GMS. This study provides an overview of how the problem of poor-quality medicines is perceived among policy actors and from this information, provides insights on what drives policy decisions. This study also offers a new application of framing analysis in health policy. Framing analysis has been a useful method to understand policy choices and to analyse the role of ideas in policy. It has also been particularly relevant in a comparative context to acknowledge variations in interpretations of a common policy problem and to inform the study of international relations, regional cooperation and cross-border policy making. This study adds to the body of literature on the application of framing analysis to policy analysis. It also proposes a three-part method for doing so – based on a stakeholder analysis, a document analysis and of semi-structured interviews. The combination of these methods elucidates the value of quality research in interpretive policy analysis – where ideas and inter-subjective interpretations of policy form an inherent part of policy making.

For the dissemination of the results, I have shared the main findings with key respondents from each country, and in the form of a report with the ethical committees of the research institutions that approved my research project. I presented the results of this thesis at three international conferences and seminars during my PhD – in Bangkok and London. I have also been given the opportunity to apply this acquired knowledge as a consultant to a development project funded by the Asian Development Bank (ADB), and as implemented by the Centre of Regulatory Excellence in Singapore on improving the regulatory capacity of NRAs in the GMS.

Acknowledging limitations

Several limitations to this study must be acknowledged. Firstly, this study was conducted independently as a PhD candidate and did not benefit from the parallel coding of an associate researcher. This incurs some risk for research bias. To mitigate these risks, I sought the advice and help of my supervisors and advisory committee to cross check the data and my analysis.

As explained in Chapter 5, I also cross-referenced my findings by validating quotations with respondents themselves.

As a French researcher in Southeast Asia, my legitimacy to conduct these interviews may have been questioned by respondents themselves. Fortunately, my previous experience conducting qualitative interviews at ministerial level in Southeast Asia was helpful to navigate these challenges. During my fieldwork, government-level respondents sometimes inquired about my ability to seek funding from donor organisations on their behalf. This was a culturally challenging development during the fieldwork. In response to such situations, I made sure to emphasise my role as an independent researcher affiliated to LSHTM throughout the interviewing process. I referred to the interviewing process and anonymity requirements to re-center the discussion as an academic interview. The language barrier constituted another limitation during my research. Although most respondents were comfortable speaking in English or French and I did not require the support of a translator, opinions were at times not expressed as clearly as they might have been if they were expressed in their mother tongue.

There are other important limitations to conducting a qualitative study as an independent researcher. Opinions and perceptions are hard to measure and analyse objectively. As regularly as was required throughout this study, I made sure to remove any pre-conceived notions of the topic of poor-quality medicines so as not to let any previous knowledge hinder the interpretation of the data collected from the semi-structured interviews. This was crucial to allow for new themes to emerge from the data. To support the qualitative data analysis process, the use of field notes and memos was crucial to record elements of the respondents' discourse that would inform my analysis of political sensitivities and potential gaps in interviewees' responses.

The potential for biased opinions due to political influences is another limitation of this qualitative study (Robson 2011). Information has been suppressed or removed from the data due to withdrawal of consent or by indirect political pressure to hide certain facts. Some respondents did not address or respond to my questions directly. To mitigate this challenge, I reviewed my questions iteratively throughout the interviewing process to guide the discussion to be as open and relevant to the topic as possible. It was essential in this respect to cross-reference information from interviews with non-government respondents to identify any potential sensitivities. From the findings of this study, it is important to note that there are various dimensions of the topic that I did not explore thoroughly, due to the limited resources available. For example, the analysis of documents was centred almost exclusively on public

health policies and laws. I did not explore criminal laws. I also did not conduct an in-depth exploration of regulatory gaps, although this came out as a strong theme in all three countries.

Observations made from the data collected in Cambodia, Lao PDR and from Thailand may not reflect what is happening in the rest of the GMS (i.e., Myanmar, Vietnam, or the south-western provinces of China) where the problem of poor-quality medicines may be interpreted very differently. Furthermore, observations on regional cooperation for this study are drawn exclusively from the accounts of respondents based in three of ten ASEAN countries only and from a document analysis. The interviews conducted included specific questions on respondents' experience and perceptions of the role and position of ASEAN on the issue of medicine quality. I did not have the opportunity for example to interview representatives from ASEAN at its headquarters in Jakarta. The observations articulated in this study are therefore conceptual generalisations only, intended to introduce a way of thinking about the problem poor-quality medicines in the GMS, rather than to extrapolate on factual interpretations of this policy problem for the whole region (Green & Thorogood 2014). Throughout this study, I acknowledged the importance of context and how this influences my analysis across the three case studies. This is to be taken into consideration if the conceptual framework is to be applied to a different regional setting. While the thematic categories drawn from the literature can guide research in a different setting, these themes should be analysed with a strong reference to contextual specificities.

Also, in terms of the generalisability of my findings to the problem of poor-quality medicines, I note throughout this study that I explore interpretations of the problem of poor-quality AMLs first and foremost. This generated conversation on the status of national malaria control efforts and the distribution of AMLs, which is conducted predominantly through vertical health programs. For this reason, the applicability of findings to other essential medicines is limited. Nevertheless, studying the case of AMLs served as a great entry point into the topic of substandard and falsified medicines.

Questions for further research

From the findings of this study, I have identified some relevant questions for further empirical research on the challenge of poor-quality medicines. Firstly, the proposed conceptual framework could be applied to a different regional setting to explore how the problem of poor-quality medicines is framed by policy actors. Secondly, in view of the salience of the security frame, it would be interesting to explore why the securitisation of the problem of poor-quality medicines has not translated into a robust policy response beyond drug safety. This would

entail a deeper exploration of regulatory challenges and gaps at the national level and a thorough analysis of the security concept in regional politics. With regards to the GMS and the ASEAN context, further research on the impact of the AEC on the policy problem of poor-quality medicines would also be relevant. Despite forecasted increases in the movement of people and goods, the AEC policies concern skilled labour first and foremost. Although respondents in this study expressed concern at the AEC as increasing the risk for the heightened circulation of illicit goods, including substandard and falsified medicines, the impact AEC may be limited, seeing as borders in the GMS are already porous.

Reflecting on the journey

The problem of poor-quality medicines came to my attention while working in health policy research on access to medicines between 2010 and 2014. While conducting a study of regional health policy in Southeast Asia and subsequently working for a foundation specialized in the supply of essential medicines in low and middle-income settings, my interest was sparked by the debates around falsified medicines, an issue still under-researched from a policy and regulatory perspective. It has been an insightful journey working on this topic from within the faculty of public health policy at LSHTM, although it has been a challenging topic to explore due to the political sensitivity and the nature of the environment in which this study was conducted. While the topic was not easy to navigate and many questions remain unanswered, below are some concluding observations from my experience conducting this study since January 2014.

The policy issue of poor-quality medicines is complex and multi-faceted and weaves in elements of political sciences, international relations, law, as well as sociology and economics. Regulatory science (understood here as the development of tools and standards for the safety and quality of medicines) encompasses both policy development and law. It was useful to apply my background in political sciences, international law and international relations to explore the policy problem of poor-quality medicines, its determinants and drivers. During my time at LSHTM, I drew from the expertise of colleagues in health policy analysis and global health research and discussed my findings with malaria experts through my membership at the LSHTM malaria center. From this, it became evident that it would be beneficial for this policy issue to be explored from an economic perspective – to determine the economic argument for dedicating time and resources towards regulatory systems strengthening to promote access to health.

Time and resources permitting, I would have spent longer in each country setting, to allow sufficient time to go through administrative processes which may have opened further doors to government level respondents. This would have been beneficial for a more in-depth understanding of the country setting as well. The fact that I was familiar with these countries prior to undertaking this study did help nevertheless. With more time in each country, I would also have worked closely with a local translator, whom I would have invited to accompany me throughout the interviewing process. This would have offered respondents the opportunity to conduct the interviews in Lao, Khmer, Thai, French or English. However, it would have required the support of a professional transcription service to translate and transcribe the recorded interviews, and would also have been more challenging to note observations from these interviews, should the respondent not consent to be recorded. Being accompanied by a local representative during these interviews might have increased my credibility towards the respondents. To this effect, I would have encouraged a member of each host organization to accompany me through this process as well. This different approach would have required more time to brief the participants on the process for conducting the interviews and on confidentiality requirements. Finally, I may also have considered hiring a local research assistant or translator to support a more thorough analysis of the legal and policy documents, in both their original versions and English translated versions. This would have permitted a closer analysis of the terminology used and the variations in definitions. Regardless, I am thrilled with the experience and believe that the knowledge acquired will be an inspiration for my ongoing career in academia and beyond, both from a methodological and conceptual standpoint. The problem of poor-quality medicines is a fascinating and timely topic, which will continue to be a policy challenge globally for as long as pharmaceuticals remain a costly and profitable commodity, and an essential one for the health and wellbeing of populations.

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Appendix 1 – Global stakeholders

Institution	Acronym	Decription
World Health Organization	WHO	The WHO works to raise awareness among the global health community about the need to improve access to quality medicines. the WHO first set up the International Medical Products Anti-Counterfeiting Taskforce and subsequently Member State Mechanism to spearhead these efforts at the national level. WHO also established a global Rapid Alert System to share pharmacovigilance information about medicine quality and product recalls. WHO hosts the WHO Prequalification Programme as a standardization for medicine quality. At the national level, WHO offices support health system development which in part works to improve the quality of health services and access to essential medicines.
United States Pharmacopeia	USP	USP is a nonprofit organization that provides technical support to nation states, in particular the ministries of health and the DRAs in the form of capacity building. USP works to improve national standards for the quality of medicines by monitoring quality in ley sentinnel sites with the use of the minilab, supporting the development of Standard Operating Procedures and working towards ISO certification for national pharmaceutical testing laboratories. USP also contributes to raising awareness about the risks of poor-quality medicines
United Nations Office for Drugs and Crime	UNODC	As an inter-governmental oragnization, UNODC tackles organized crime including the illicit trade in 'fraudulent' medicines. Initiativess spearheaded by UNODC include the Container Control Programme (CCP) where UNODC works with national customs offices at ports of entry to verify the quality of the merchandise and reliability of the documentation. UNODC also worked to develop a model law against the pharmaceutical crime with the support of IRACM (see below).
International Criminal Police Organization	INTERPOL	An international law enforcement organization working with police and customs officials across national settings. Its department of pharmaceutical crime works against the illicit trade in falsified medicines. INTERPOL conducts yearly raids on these organized criminal networks working hand in hand with national law enforcement bodies. It track and arrest criminal networks of poor-quality

		medicines in Southeast Asia among other regional settings.
International Federation of pharmaceutical Manufacturers Associations	IFPMA	An internationals federation or associations representing pharmaceutical companies and based in Geneva. It contributes expertise to the global health community to improve global health including acccess to quality medicines.
International Institute of Research Against Counterfeit Medicines	IRACM	A research organization launched in France in 2010 and aimed at raising awareness and disseminating information about the threat of poor-quality medicines among government officials worldwide. IRACM conducts trainings with policy and customs officials on request.
World Trade Organization	WTO	A global International organization establishing rules for trade between countries. It also acts as a forum for countries to negotiate trade arrangements. Member states of the WTO signed an international Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) establishing rules and regulations for patent protections for pharmaceutical products. This has been perceived as a challenge to acccess to more affordable, generic medicines. Subsequently, WTO introduced flexibility tools around the TRIPS agreement to support access to medicines.
World Intellectual Property Organization	WIPO	WIPO is a global forum for intellectual property services of products operating under the United Nations as a self-funding agency. It also covers IP services for pharmaceutical products.
Global Fund to Fight Aids, Tuberculosis and Malaria	GF	A global health partnership organization established to mobilize financial resources to support efforts agains three infectious diseases - Aids, Tuberculosis and Malaria. Through its financing mechanisms, the GF broadly supports health systems strengthening including efforts to improve the regulation of pharmaceuticals.

Table 21 Global Stakeholders

Appendix 2 - Statistics on prevalence of substandard and falsified medicines in the GMS

Antimalarial drugs have been knowingly falsified in Southeast Asia since 1998 (P. N. Newton et al. 2008). It has been estimated that fake anti-malarials contribute to nearly 450,000 preventable deaths every year (Karunamoorthi 2014). In China, between 200,000 and 300,000 people die each year due to counterfeit or substandard (Primo-Carpenter 2004). This trend however is not new; Tabernero and colleagues (2014) mention that there have been reports of falsified cinchona bark in the 1600s and falsified quinine from the 1800s. While data remains scarce and we do not have a clear idea of the magnitude of the problem of falsified antimalarial drugs today (Tabernero & Newton 2012; Tabernero, Fernández, et al. 2014), some studies suggest that the problem exists and represents an important public health challenge (Newton, Amin, et al. 2011). Recent estimates for that the total prevalence of falsified antimalarial drugs in the GMS range between 33% and 53% (P. N. Newton et al. 2008; Nayyar et al. 2012; Dondorp et al. 2004). However, it is crucial to interpret these figures critically and to understand how data is collated and the surveying strategies used in the relevant studies.

Nayyar and colleagues (2012) review existing data on the prevalence of falsified antimalarial drugs in African and Southeast Asia between 1999 and 2010. Out of a sample of 939 antimalarial drugs from six studies in the GMS that carried out both chemical and packaging analysis, it appears that 448 (or 47.7%) were classified as falsified. The review offered by Nayyar *et al*. however is not extensive and only looks at six studies. Furthermore, the authors only include in their calculation samples where measuring falsification was done by both chemical and packaging analysis. The authors note that for various studies, packaging analysis was not always possible due to the difficulty of obtaining genuine samples of the original drug packaging.

Another review of evidence on the presence of falsified antimalarial drugs was conducted by the Antimalarial Quality Scientific Group between until 2014. The Antimlarial Quality Scientific Group systematically reviewed a series of scientific and lay reports on poor quality antimalarial drugs at the global level. The data is represented in an interactive map available online at the Worldwide Antimalarial Resistance Network; the Antimalarial Quality Surveyor (AQ Surveyor[63]), "an open access, web-based visualization tool that tabulates and maps

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[63] The AQ Surveyor available at http://www.wwarn. org/aqsurveyor/ is "an open access, web-based visualization tool that tabulates and maps published reports on the quality of anti-malarial medicines"

published reports on the quality of anti-malarial medicines" (Tabernero, Fernández, et al. 2014; Tabernero & Newton 2012; Worlwide Artemisinin Resistance Network n.d.). Figures on the existence of poor-quality antinalarials in the AQ surveyor can be viewed according to quality classification, whether substandard or falsified. For this study, I have reviewed the data available on the AQ Surveyor for falsified antimalarial drugs[64]. At the global level, the AQ surveyor assesses 130 studies. Out of the 9,348 anti-malarial samples tested, 30.1% failed chemical and packaging quality tests and were thus qualified as falsified (Tabernero et al. 2014).

For the GMS only, Tabernero *et al*. systematically review 19 studies that provide evidence of the presence of falsified antimalarial drugs in the, (this is including the Southern provinces of China). The 19 studies sampled six different kinds of antimalarial drugs including Artemether, Artesunate, Chloroquine, Mefloquine, Primaquine, Quinine. Global data on ACT falsification is scarce and there is only one report in the AQ Surveyor that accounts for the seizure of fake ACTs produced in China for sale in Africa (Newton et al. 2011; Tabernero et al. 2014). The types of studies reviewed include NRA seizures, lab collections, case reports, convenience sampling and random sampling surveys. To obtain a valid estimate of the total percentage of falsified antimalarial drugs in the GMS, I removed data from NRA seizures – thereby excluding one report of the seizure by INTERPOL of 56,000 fake artesunate tablets in the Yunnan Province of China which would thwart any estimate. This first result suggests that 55.4% of antimalarials are falsified. When removing data collated from lab collections as well as DRA seizures, thus keeping figures from studies with convenience or random sampling strategies as well as rare case reports, the percentage of antimalarial falsified is at 34.1% (See table 1 p. 3 for an overview of the figures from the AQ Surveyor).

For a country overview of falsification rates, I have thereafter split the data to obtain the following estimates from the AQ Surveyor: Cambodia 23.1%, Vietnam 78.2%, Lao PDR 63%, Myanmar (Burma) 30.8%, Thailand 30.4% and China (Southern Provinces) 24%. It is important to note here that very few studies were conducted in Vietnam (3 studies and 82 samples) and Myanmar (2 studies and 99 samples). Furthermore, the data available on the prevalence rates in the Southern Provinces of China are based mainly on case reports except for the convenience sample survey by Phanouvong (2005). Nevertheless, data from drug seizures in the Southern China are interesting in that they provide some evidence of these provinces being a hub for fake medicine production. Chow reinforces this statement by

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(Tabernero, Fernández, et al. 2014; Tabernero & Newton 2012; Worlwide Artemisinin Resistance Network n.d.)

[64] As of January 2015.

suggesting that most counterfeiting including pharmaceutical counterfeiting occurs in the South western China (Chow 2003) and thus conveniently very close to the borders with the rst of the GMS member states. In fact Newton and colleagues (2008) in a collaborative forensic investigation into fake antimarial drugs in the region, traced some falsified artesunate batches back to the Yunnan province of South China where a large marjority of fake antimalrials originate from, often bearing the fake hologram of the manufacturer 'Guilin Pharmaceutical' (Hall et al. 2006) (Dondorp et al. 2004).

Tabernero and colleagues (2014) note that 5-15% of member states regularly report such cases to the WHO. Although growing awareness about the problem has encouraged more scientists since 1998 to conduct studies on fake antimalarial drugs, there is still a general lack of reporting from member states and thus, we still possess insufficient data for accurate estimates. While the data collated by in the AQ Sruveyor offers some useful evidence of the existence of the problem in certain regions, there are many inconsistencies worth acknowledging regarding the existing pool of studies. Firstly, studies vary in terms of the sampling strategies used. As Tabernero and colleagues note; "estimates vary greatly depending on the sampling methodology and the technique used, probably greatly influencing reported failure rates." (2014, p.9). Few reports are based on randomized sampling strategies which is considered the "gold standard" in measuring disease prevalence for example (Tabernero et al. 2014, p. 9). Out of the studies available for the GMS on the AQ Surveyor, only half were either convenience sampling[65] or random[66] sampling surveys. Furthermore, there are many inconsistencies in the existing studies with regards to the definition of 'falsified' vs. 'substandard' drugs and how the two categories of drugs are differentiated in each survey. Classifying a drug as falsified as opposed to substandard is important however, as it implies different policy. In total, 74% of the 251 of studies reviewed for the AQ Survey did not offer a definition (Tabernero et al. 2014). In order to classify a drug as falsified however, both chemical analysis and packaging analysis are required. This is one way to discern a criminal intent as opposed to a manufacturing error. At times however, the possibility of obtaining a sample package of the original drug proves too difficult, and drugs are classified as falsified based on the lack of or incorrect amounts of API – this may lead to some inaccurate estimates (Tarbernero et al. 2014; Nayyar et al. 2012). We do not as of yet possess data from a systematic, comprehensive, region-wide random sampling surveys available for an accurate estimate of prevalence of falsified antimalarial drugs in the region (Johnston & Holt 2014). Nevertheless, the data

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[65] Convenience sample surveys: (Dondorp et al. 2004; Lon et al. 2006; Newton et al. 2001; Phanouvong et al. 2005; Shakoor et al. 1997; Rozendaal 2001b)
[66] Random sample surveys: (Sengaloundeth et al. 2009; Phanouvong, Raymond, Krech & Dijiba 2013)

available on the AQ Surveyor provides a good indication that falsified antimalarial drugs are a problem in the GMS.

Table 22 Results from AQ Surveyor on % Falsified antimalarial drugs in the GMS member states

Country	Study (authors)	Survey type	Antimalarial	Sample	% falsified	No. of falsified
Cambodia	Aldhous 2005	Case Reports	Mefloquine	1	100	1
Cambodia	Bagozzi D 2003	Case Reports	Artesunate	unknown	100	unknown
Cambodia	Dondorp A.M. 2004	Convenience	Artesunate	22	23	5.06
Cambodia	Hall K.A. 2006	Laboratory collections	Artesunate	6	50	3
Cambodia	Lon 2006	Convenience	Artesunate	81	20	16.2
Cambodia	Lon 2006	Convenience	Chloroquine	94	1	0.94
Cambodia	Lon 2006	Convenience	Mefloquine	39	8	3.12
Cambodia	Lon 2006	Convenience	Quinine	85	71	60.35
Cambodia	Newton 2001	Convenience	Artesunate	26	25	6.5
Cambodia	Newton 2008	Laboratory collections	Artesunate	48	100	48
Cambodia	Phanouvong 2005	Convenience	Artesunate	32	25	8
Cambodia	Phanouvong 2005	Convenience	Chloroquine	54	2	1.08
Cambodia	Phanouvong 2005	Convenience	Mefloquine	21	5	1.05
Cambodia	Phanouvong S 2013	Random	Artesunate	25	12	3
Cambodia	Phanouvong S 2013	Random	Quinine	25	20	5
Cambodia	Rozendaal 2000	Case Reports	Mefloquine	3	100	3
Cambodia	Rozendaal 2001	Convenience	Artesunate	3	66	1.98
Cambodia	Phanouvong 2005	Convenience	Quinine	25	44	11
China (Dongxing)	People's Daily Online	Case Reports	Chloroquine	unknown	100	unknown
China (Dongxing)	People's Daily Online	Case Reports	Primaquine	unknown	100	unknown
China (Guangzhou)	Faucon B. 2013	DRA Seizure	Artemether	600	100	600
China (Yunnan)	Newton et al. 2008	DRA Seizure	Artesunate	56000	100	56000
China (Yunnan)	Phanouvong 2005	Convenience	Artesunate	18	17	3.06
China (Yunnan)	USP 2004	Case Reports	Artesunate	3	66	1.98
Lao	Alter K. 2004	Laboratory collections	Artesunate	16	100	16
Lao	Dondorp A.M. 2004	Convenience	Artesunate	46	54	24.84
Lao	Newton 2001	Convenience	Artesunate	8	38	3.04

Lao	Newton 2008	Laboratory collections	Artesunate	115	100	115
Lao	Phanouvong 2005	Convenience	Artesunate	8	37	2.96
Lao	Sengaloundeth 2009	Random	Artesunate	2	100	2
Lao	Sengaloundeth 2009	Random	Artesunate	4	100	4
Lao	Sengaloundeth 2009	Random	Artesunate	4	75	3
Lao	Sengaloundeth 2009	Random	Artesunate	11	100	11
Lao	Sengaloundeth 2009	Random	Artesunate	3	100	3
Lao	Sengaloundeth 2009	Random	Artesunate	1	100	1
Myanmar	Dondorp A.M. 2004	Convenience	Artesunate	48	21	10.08
Myanmar	Hall K.A. 2006	Laboratory collections	Artesunate	2	50	1
Myanmar	Ministy of Health 2001	DRA Seizure	Artemether	1	100	1
Myanmar	Newton 2001	Convenience	Artesunate	51	40	20.4
Myanmar	Newton 2006	Case Reports	Artesunate	1	100	1
Myanmar	Newton 2008	Laboratory collections	Artesunate	137	100	137
Thailand	Dondorp A.M. 2004	Convenience	Artesunate	11	27	2.97
Thailand	Newton 2001	Convenience	Artesunate	8	11	0.88
Thailand	Newton 2008	Laboratory collections	Artesunate	16	100	16
Thailand	Shakoor 1997	Convenience	Chloroquine	5	60	3
Vietnam	Dondorp A.M. 2004	Convenience	Artesunate	61	92	56.12
Vietnam	Hall K.A. 2006	Laboratory collections	Artesunate	2	60	1.2
Vietnam	Newton 2001	Convenience	Artesunate	11	64	7.04
Vietnam	Newton 2008	Laboratory collections	Artesunate	75	100	75
Vietnam	Phanouvong 2005	Convenience	Artesunate	10	10	1

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Appendix 3 – Literature Review Chapter - List of References

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Appendix 4 – Topic Guide

LONDON
SCHOOL of
HYGIENE
&TROPICAL
MEDICINE

Project Title: **Framing the challenge of falsified and substandard medicines: the case of poor-quality antimalarial drugs in Cambodia, Laos and Thailand.**

Topic Guide

General Questions
- How do you understand the problem of fake drugs?
- What do you think is the main reason why we can find fake antimalarial drugs in this country?
- Do you think it is an important issue to tackle today?
- Do you think that it is particularly urgent in the GMS and why?

Country Specific Questions
- What are the main initiatives in this country to tackle the problem of fake drugs
- What is your opinion on the work of this country to tackle fake medicines?
- What is the role of the *National Regulatory Authority*?
- What is the role of the police?
- What is the role of customs organizations
- Do these organizations work together?
- Are there any recent prosecutions or seizures you can think of?

Questions on access to medicines and consumer behavior
- How does access to medicines work in this country - and do you think any of these elements impact the trade in fake drugs?
- How do patients obtain antimalarial drugs in this country?

Questions on regional initiatives
- Is there any regional initiative you can think of that is relevant to curbing the trade in fake drugs
- What is the role of ASEAN in all of this?
- Do you think free trade with neighboring countries has an impact on the trade in fake drugs?
- What will it be in 2015, after the ASEAN Economic Community is set up?

Closing question
- In your opinion what would be the best way forward to tackle the problem of fake antimalarial drugs in this region?

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Appendix 5 – Ethics approvals

Observational / Interventions Research Ethics Committee

LSHTM

6 March 2015

Dear

Study Title: Understanding and explaining the high prevalence of falsified antimalarial drugs in the Greater Mekong Subregion of Southeast Asia.

LSHTM Ethics Ref: 8814

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Advertisements	Generic Email to Respondents	18/12/2014	1
Investigator CV	CV - 1p - Marie Lamy 2015 LSHTM	18/12/2014	1
Information Sheet	LSHTM Ethics Application – information sheet and Consent form	13/01/2015	3
Protocol / Proposal	Study Protocol - falsified antimalarials GMS - LAMY	13/01/2015	2
Local Approval	Approval Letter 20150108	04/03/2015	1
Covering Letter	Cover letter to LSHTM Ethics Committee	05/03/2015	2
Protocol / Proposal	Study Protocol - falsified antimalarials GMS - LAMY	05/03/2015	3
Local Approval	Lao Ethics Approval 20150304	05/03/2015	1

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

USER
You are logged in as...
marielamy
• My Profile
• Log Out

NOTIFICATIONS
• View

Home > User > Investigator > Submissions > #386 > **Summary**

2015.4.NIOPH.4.MC Summary / ສະຫລຸບ/ສ່ງວວນທຍ,

SUMMARY / ສະຫລຸບ/ສ່ງວວນທຍ,   REVIEW / ທບທວນ

Submission / ການສຶ່ງບົດສະ ຫນ4

Investigator(s)	Marie Clemence Michelle Lamy
Proposal ID / ລະ ຫັດບົດສະ ຫນ4	2015.4.NIOPH.4.MC
Title / ຫົວຂ໋,	Understanding and explaining the high prevalence of falsified antimalarial drugs in the Greater Mekong Subregion, Southeast Asia
Proposal file / ໄຟລບົດສະ ຫນ4	2015.4.NIOPH.4.MC.MAINPROPOSAL.5.FEB202015-2:13AM.PDF
Supp. Files / ໄຟລເພ່ ມບົດມູນເພ່ມ	2015.4.NIOPH.4.MC.SUPPLEMENTARYFILE1.1.JAN082015-11:52PM.PDF (CV of Principal Investigator) 2015.4.NIOPH.4.MC.SUPPLEMENTARYFILE2.1.JAN082015-11:52PM.DOCX (Questionnaires) 2015.4.NIOPH.4.MC.SUPPLEMENTARYFILE3.1.FEB202015-2:14AM.DOCX (Informed Consent) 2015.4.NIOPH.4.MC.SUPPLEMENTARYFILE4.1.FEB202015-2:15AM.PDF (Letter from Institution (LSHTM)) 2015.4.NIOPH.4.MC.SUPPLEMENTARYFILE5.1.FEB202015-2:15AM.PDF (Summary) 2015.4.NIOPH.4.MC.SUPPLEMENTARYFILE6.1.FEB202015-2:16AM.JPG (Other ERC Decision) 386-1909-1-SUPPLEMENTARYFILE.PDF (Final Decision)
Submitter / ຜຸ້ສຶ່ງບົດສະ ຫນ4	Ms Marie Clemence Michelle Lamy
Date submitted / ວັນທ່ສຶ່ງບົດສະ ຫນ4	February 20, 2015 - 02:22 AM
Investigator comments	Dear Sir/Madam, Thank you for your comments on my first submission. I have now resubmitted my application to the NECHR and I have included a Summary Abstract of 2 pages (in English and Lao) of my study. I have also attached a letter of support which includes the signature of my Host institution in Lao PDR; the Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit. I was also able to include a letter of approval from the NECHR in Cambodia, for your further information. Please note that due to some changes in the planning of my fieldwork, the dates of my first visit to Southeast Asia have changed (to March/April 2015). This has not been corrected in the Lao version, thank you for taking into account the dates stated in the English version of the protocol. Please let me know if you have received my payment of 50 USD for this application. I look forward to hearing back from you and I thank you for your time and consideration, Kind Regards, Marie Lamy

Status / ສະ ຖານະ

Status / ສະ ຖານະ	Approved
Date / ວັນທ4	2015-03-05

Investigator(s)

Investigator / [?] ຜ໋ຮັບຜິດຊອບການວິໄຈທ່	Marie Clemence Michelle Lamy Marie.Lamy@lshtm.ac.uk London School of Hygiene and Tropical Medicine, London, United Kingdom 00447909671754

Proposal Details / ສະ ຫລວບ/ສ່ງວວນທຍ,

Scientific title [?] ຫົວຂໍ້ຫຼະ ທາງ	Understanding and explaining the high prevalence of falsified antimalarial drugs in the Greater Mekong Subregion, Southeast Asia
Public title [?] ຫົວຂໍ້ທົ່ວໄປ	Understanding and explaining the high prevalence of falsified antimalarial drugs in the Greater Mekong Subregion, Southeast Asia
Student research [?] ການວໄຈທ່ເປັນຂອງນັກຮຽນ	Yes
	Institution / [?] ສູງາບັນ/ສະ ຖານ ບ : London School of Hygiene and Tropical Medicine Academic degree: / [?] ລະ ດັບຄວາມ ຮຽນ : Ph.D

| Abstract
 [?] ບົດຄົດຫຍ່, | The World Health Organization (WHO) estimates the global market in fake medicines to be in excess of US$75 billion. The illicit trade in fake drugs represents a pressing public health concern. The Greater Mekong Subregion (GMS) in particular, has one of the world's largest concentrations of falsified medicines, especially of antimalarial and tuberculosis drugs. Falsified or fake drugs may contain none, or inadequate quantities of the Active Pharmaceutical Ingredient (API), or may contain harmful ingredients. This poses a considerable threat to human lives and an obstacle to infectious disease control, also due to the associated risk of antimicrobial resistance. Despite past efforts from GMS governments to tackle this issue, and regardless of lower prevalence rates of fake antimalarial drugs estimated in Thailand, Lao PDR and Cambodia, the problem of fake medicines persists. We still have a limited understanding of the reasons why fake antimalarial drugs are still prevalent in the GMS. Additionally, there is no comprehensive study evaluating the governance landscape of Southeast Asia with regards to falsified medicines. As trade liberalization in Southeast Asia intensifies, there are concerns that reduced custom controls and higher mobility of people and goods may cause further increase in this illicit trade. In this context, it is crucial to understand the complexity of this multi-faceted public health challenge. This exploratory study will address an apparent gap in the literature by providing empirical evidence of the factors that contribute to a high prevalence of falsified antimalarial drugs in the GMS. This study makes use of qualitative research methods to evaluate the perceptions of relevant stakeholders on this phenomenon, and to evaluate the way in which existing regulatory and governance mechanisms in the GMS respond to the challenge of fake antimalarial drugs. The findings from a thorough document analysis and from a series of semi-structured interviews will bring further insight into the challenge of fake antimalarial drugs in Southeast |

สำนักงานคณะกรรมการวิจัยแห่งชาติ
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โทรศัพท์ 66-2940-6369, 66-2561-2445 ext. 454
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Website : http://foreignresearcher.nrct.go.th

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BANGKOK 10900, THAILAND
Telephone 66-2940-6369, 66-2561-2445 ext. 454
Fax 66-2561-3049
Email: webmaster@nrct-foreignreseacher.org

วช.
NRCT

No. 0002/6519

14 August B.E. 2558 (2015)

Dear Ms. Lamy,

Please refer to your request for conducting research in Thailand in a project entitled "Understanding and Explaining Falsified Antimalarial Drugs in the Greater Mekong Subregion, Southeast Asia". Having consulted the Thai Food and Drug Administralion, the Bureau of Vector-borne Diseases, the Bureau of Drugs and Narcotics, the Government Pharmaceutical Organization and the Customs Department about data collection, we are pleased to inform you that you are allowed to conduct research in Thailand in the above mentioned project for the period of September 2015 to October 2015.

With regard to an immigration regulation, it is recommended that you contact the Royal Thai Embassy to obtain non-immigrant visa (RS) before arriving in Thailand. Please note that you would be requested to contact NRCT's officials at the Foreign Researcher Management Section, the Division of International Affairs, NRCT (1st Floor, 3-storey building) within seven days after your arrival in Thailand in order to obtain concerned documents and to pay a deposit of THB 10,000 for guaranteeing a submission of your complete report. A map of NRCT with NRCT's office hours is attached herewith for your information.

Should you have any queries or concerns, please do not hesitate to contact us at webmaster@nrct-foreignreseacher.org or Tel.+66-2-561 2445 ext. 454.

We are looking forward to welcoming you.

Sincerely yours,

(Mr. Kristhawat Nopnakeepongse)
Deputy Secretary - General
for Secretary – General

Ms. Marie Lamy
Flat 303 Dryden Building
37 Commercial Road
E1 1LF
United Kingdom

Encl.

KINGDOM OF CAMBODIA
ជាតិ សាសនា ព្រះមហាក្សត្រ
NATION RELIGION KING

MINISTRY OF HEALTH

National Ethics Committee for Health Research

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Ms. Marie LAMY

Project: Understanding and explaining falsified antimalarial drugs in the Greater Mekong subregion, Southeast Asia. Version N° 1, dated 17th December, 2014

Reference: - Your letter received on 14th December, 2014
- Report of NECHR's secretaries on 5th January, 2015

Dear Ms. Marie LAMY,

I am pleased to notify you that your study of the protocol entitled "Understanding and explaining falsified antimalarial drugs in the Greater Mekong Subregion, Southeast Asia. Version N° 1, dated 17th December, 2014" has been approved by National Ethic Committee for Health Research (NECHR). This approval is valid for twelve months after the approval date.

The Principal Investigator of the project shall submit following document to the committee's secretariat at the National Institute of Public Health at #2 Kim Il Sung Blvd, Khan Tuol Kork, Phnom Penh. (Tel: 855-23-880345, Fax: 855-23-881949):

- Annual progress report
- Final scientific report
- Patient/participant feedback (if any)
- Analyzing serious adverse events report (if applicable)

The Principal Investigator should be aware that there might be site monitoring visits at any time from NECHR team during the project implementation and should provide full cooperation to the team.

Regards,

Chairman

Prof. ENG HUOT

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Appendix 6 – Information sheet and consent form

Participant Information sheet

Project Title: **Framing the challenge of falsified and substandard medicines: the case of poor-quality antimalarial drugs in Cambodia, Laos and Thailand.**

My name is Marie Lamy, I am a graduate student at the London School of Hygiene and Tropical Medicine, doing research in the Department of Global Health and Development. I am conducting a study about fake antimalarial medicines in the Greater Mekong Subregion, including (insert relevant country here). The aim of this study is to better understand why fake antimalarial drugs are present in this region. Hopefully, the outcome of this research project can inform the development of new policies and legal mechanisms to guarantee the safety of malaria patients. I hope this project can also help other researchers understand more about the fake medicine market in other regional settings.

I will be interviewing stakeholders in the Greater Mekong Region during two fieldwork sessions; one this month (March 2015) and another in September 2015. I will be speaking with a variety of people ranging from policy makers, policy and customs officials, and researchers, to members of international organizations.

I am conducting this study independently, and no other organisation is directly involved in this research. All data collected during my fieldwork will remain anonymous and confidential. If you agree to proceed with this interview, I will ask if it is possible to record our conversation today. If you are not comfortable with this, please let me know and I will not turn on the

recorder. The information I gather from the interviews is stored securely and remains fully confidential.

If you agree to proceed, this interview will take approximately one hour. You can decline to answer a question at any point during the interview. You are also free to stop the interview at any time. If you wish to withdraw your participation from this study you can do so at any time, even after this interview. Finally, if you want to continue to discuss any of the issues that come up during our conversation, you are free to contact me by email or by telephone. My contact details are available below.

Thank you for your time,

Marie Lamy

Email address: Marie.Lamy@lshtm.ac.uk
UK number: +44 (0)7909 671 754

Informed consent form

LONDON
SCHOOL *of*
HYGIENE
&TROPICAL
MEDICINE

Project Title: **Framing the challenge of falsified and substandard medicines: the case of poor-quality antimalarial drugs in Cambodia, Laos and Thailand.**

Informed Consent Form

Study Title: *Understanding and Explaining the high prevalence of falsified antimalarial drugs in the Greater Mekong Subregion, Southeast Asia*

Researcher: Marie Lamy (London School of Hygiene and Tropical Medicine)
Name of Respondent:
Respondent ID:

Please

initial box

1. I have read and understood the attached information sheet giving details of the project. I have had the opportunity to consider the information, ask questions and have had these answered fully.	
2. Marie Lamy has explained to me the nature and purpose of this interview.	
3. I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason.	
4. I understand that the collected data as audio records and transcripts will be stored in secure storage.	
5. I understand that data gathered in this project may form the basis of a report or other form of publication or presentation, and that my personal information will be protected by strict adherence to anonymity and confidentiality.	
6. I agree to take part in the above study	

If you agree to take part, please tick (only) one box as appropriate:

[ ] I agree to take part in this interview, and for quotes and other material arising from my participation to be used and attributed by name.

(Note, individual statements can still be requested to remain anonymous during the interview)

[ ] I agree that material from my interview may be quoted, but I would like my name to be anonymised.

[ ] I agree that material from my interview may be quoted, but I would like my name to be anonymised as well as any other information that might be used to identify me, including the organisation that employs me and my position within it.

[ ] I do not agree that any material from my interview may be quoted, but the researchers may use information from my interview to inform their analysis.

Attachment: Information Sheet

Respondent Name:

Signature:

Date:

Researcher Name:

Signature:

Date:

Appendix 7 – Coding framework

Economic determinants

- Demand and supply
- Globalization and trade liberalisation
- Development status (Low and middle-income countries)
- Profit making business

Socio-cultural determinants

- Attitudes towards counterfeit products
- Consumer behaviour / health-seeking behaviour

Legal challenges

- Complex organised crime
- Lack of targeted laws
- No global definition
- Rule of law and enforcement

Regulatory challenges

- Lack of cooperation among stakeholders
- Capacity and capability of NRAs

Socio-economic drivers

- Globalization and trade
- Demand and supply
- Consumer perception and awareness of risk

Political drivers

- Power dynamics
- Lack of political will and corruption
- Donor priorities

Health systems issues

- Health service delivery and infrastructure
- Health-seeking behaviour

- Supply chain of pharmaceuticals

Note that some of these sub themes were included as free nodes in Nvivo, or themes that emerged progressively from the data.

Appendix 8 – List of respondents

Locally based policy actors

Respondent Code	Category	Organization Type	Recorded	Date	Location	Consent
STK01NG_INGO20150330	Non-government	International Non-governmental Oragnisation	No	30/03/2015	Phnom Penh	1
STK02NG_INGO20150331	Non-government	International Non-governmental Oragnisation	Yes	31/03/2015	Phnom Penh	1
STK03NG_Consult20150331	Non-government	Consultant	Yes	31/03/2015	Phnom Penh	2
STK04NG_INGO20150321	Non-government	International Non-governmental Oragnisation	Yes	31/03/2015	Phnom Penh	1
STK05NG_IGO20150401	Non-government	Inter-governmental Oragnisation	Yes	01/04/2015	Phnom Penh	1

STK06NG_Donor20150401	Non-government	Donor Organisation	Yes	01/04/2015	Phnom Penh	1
STK07G_NRA20150401	Government	National Regulatory Agency	No	01/04/2015	Phnom Penh	1
STK08NG_LNGO20150402	Non-government	Local Non-governmental Organisation	Yes	02/04/2015	Phnom Penh	1
STK09NG_LNGO20150402	Non-government	Local Non-governmental Organisation	Yes	02/04/2015	Phnom Penh	3
STK10G_NMCP20150402	Government	National Malaria Control Program	No	02/04/2015	Phnom Penh	4
STK11NG_IGO20150403	Non-government	Inter-governmental Oragnisation	Yes	03/04/2015	Phnom Penh	3
STK12NG_Donor20150403	Non-government	Donor Organisation	No	03/04/2015	Phnom Penh	3
STK13NG_Donor20150403	Non-government	Donor Organisation	No	03/04/2015	Phnom Penh	4

STK14NG_IGO20150404	Non-government	Inter-governmental Oragnisation	No	04/04/2015	Phnom Penh	2
STK15NG_INGO20150404	Non-government	International Non-governmental Organisation	Yes	04/04/2015	Phnom Penh	3
STK16NG_INGO20150404	Non-government	International Non-governmental Organisation	NA	NA	Phnom Penh	NA
STK17NG_INGO20150406	Non-government	International Non-governmental Organisation	No	06/04/2015	Phnom Penh	3
STK18NG_Donor20150406	Non-government	Donor Country	No	06/04/2015	Phnom Penh	4
STK20G_NRA20150407	Government	National Regulatory Agency	No	07/04/2015	Vientiane	4
STK21G_NRA20150408	Government	National Regulatory Agency	Yes	08/04/2015	Vientiane	1
STK23G_NRA20150508	Government	National Regulatory Agency	Yes	08/04/2015	Vientiane	1

STK24G_NRA20150508	Government	National Regulatory Agency	No	08/04/2015	Vientiane	2
STK25G_NRA20150508	Government	National Regulatory Agency	Yes	08/04/2015	Vientiane	1
STK26NG_INGO20150409	Non-government	International Non-governmental Organisation	Yes	09/04/2015	Vientiane	2
STK27G_LEA20150409	Government	Law Enforcement Agency	No	09/04/2015	Vientiane	4
STK28NG_Pharma20150409	Non-government	Pharmaceutical Manufacturer	No	09/04/2015	Vientiane	4
STK29G_NRA20150410	Government	National Regulatory Agency	No	10/04/2015	Vientiane	1
STK30G_MoH20150410	Government	Ministry of Health	Yes	10/04/2015	Vientiane	1
STK31NG_IGO20150410	Non-government	Inter-governmental Oragnisation	Yes	10/04/2015	Vientiane	4

STK32NG_IGO20150410	Non-government	Inter-governmental Oragnisation	Yes	10/04/2015	Vientiane	4
STK34NG_Academia20150410	Non-government	Academia	No	10/04/2015	Vientiane	4
STK35NG_Donor20150410	Non-government	Donor Organisation	No	10/04/2015	Vientiane	4
STK36NG_Academia20150413	Non-government	Academia	Yes	13/04/2015	Vientiane	1
STK37G_NCMP20150413	Government	National Malaria Control Program	Yes	13/04/2015	Vientiane	4
STK38NG_Academia20150413	Non-government	Academia	No	13/04/2015	Vientiane	
STK39NG_Academia20150417	Non-government	Academia	No	17/04/2015	Singapore	
STK40G_NMCP20150603	Government	National Malaria Control Program	Yes	03/06/2015	Bangkok	1
STK41NG_Academia20150605	Non-government	Academia	Yes	05/06/2015	Bangkok	1

STK42NG_Academia20150605	Non-government	Academia	Yes	05/06/2015	Bangkok	2
STK43G_LEA20150605	Government	Law Enforcement Agency	Yes	05/06/2015	Bangkok	1
STK44G_MoH20150609	Government	Ministry of Health	Yes	09/06/2015	Bangkok	2
STK45G_LEA20150609	Government	Law Enforcement Agency	No	09/06/2015	Bangkok	1
STK46NG_IGO20150610	Non-government	Inter-governmental Oragnisation	No	10/06/2015	Bangkok	2
STK47NG_20150915	Non-government	Pharmaceutical Manufacturers Association	Yes	15/09/2015	Bangkok	3
STK48NG_LNGO20150907	Non-government	Local Non-governmental Organisation	Yes	07/09/2015	Bangkok	1
STK49G_NRA20150911	Government	National Regulatory Agency	Yes	11/09/2015	Bangkok	1
STK50G_NRA20150911	Government	National Regulatory Agency	Yes	11/09/2015	Bangkok	1

STK51NG_Academia20150916	Non-government	Academia	Yes	16/09/2015	Bangkok	1
STK52NG_Pharma20150910	Non-government	Pharmaceutical Manufacturer	Yes	10/09/2015	Bangkok	1
STK53NG_Pharma20150910	Non-government	Pharmaceutical Manufacturer	Yes	10/09/2015	Bangkok	1
STK54NG_INGO20150910	Non-government	International Non-governmental Organisation	Yes	10/09/2015	Bangkok	3
STK55NG_INGO20150910	Non-government	International Non-governmental Organisation	Yes	10/09/2015	Bangkok	3
STK56G_20150914	Government	Law Enforcement Agency	No	14/09/2015	Bangkok	1

Expert Respondents

Code	Category	Recorded	Interview Type	Date	Location	Consent
EXP01_Other20151027	Other	No	Email	01/27/2015	London	2
EXP02_Academia20150203	Academia	No	In Person	03/02/2015	London	2
EXP03_IGO20150411	Inter-Governmental Organisation	Yes	Skype	11/04/2015	France	2
EXP04_INGO20150224	International Non-governmental Oragnisation	Yes	Skype	24/02/2015	Washington D.C.	2
EXP05_Academia20150318	Academia	Yes	In Person	18/03/2015	France	2
EXP07_Academia20150616	Academia	No	Skype	16/06/2016	Paris	2
EXP08_INGO20150224	International Non-governmental Oragnisation	Yes	Skype	24/02/2015	Washington D.C.	2

EXP09_Donor20150224	Donor Organisation	Yes	Skype	24/02/2015	Washington D.C.	2
EXP10_Academia20150303	Academia	Yes	Skype	03/03/2015	Australia	2
EXP11_Academia20150410	Academia	No	Skype	10/04/2015	Unknown	1
EXP12_INGO20150317	International Non-governmental Oragnisation	Yes	Skype	17/03/2015	Netherlands	2
EXP13_Academia20150416	Academia	Yes	Skype	16/04/2015	Japan	2
EXP14_IGO20150331	Inter-Governmental Organisation	Yes	Skype	31/03/2015	Beijing	2
EXP15_INGO20150624	International Non-governmental Oragnisation	Yes	Skype	24/06/2015	Washington D.C.	2
EXP17_INGO20150716	International Non-governmental Oragnisation	Yes	in Person	16/07/2015	Washington D.C.	2
EXP18_Academia20150407	Academia	No	in Person	07/04/2015	London	2

EXP21_Pharma20150624	Pharmaceutical Industry	Yes	Skype	24/06/2015	Paris	2
EXP22_Pharma20150629	Pharmaceutical Industry	Yes	Skype	29/06/2015	Basel	2
EXP24_Pharma20150720	Pharmaceutical Industry	No	in Person	20/07/2015	London	2
EXP25_INGO20150930	International Non-governmental Oragnisation	Yes	Skype	30/09/2015	Geneva	2
EXP26_Donor20150806	Donor Organisation	No	Skype	06/08/2015	Seattle	2
EXP28_Pharma20151021	Pharmaceutical Industry	Yes	Skype	21/10/2015	Geneva	3
EXP29_Pharma20160623	Pharmaceutical Industry	No	in Person	23/06/2016	London	2

Appendix 9 – Cambodia pharmaceutical regulatory system

Procurement of medicines

For the procurement of medicines, Operational District Medical Stores (ODMS) assess the need for medicines through a process of quantification and relay the information to the Essential Drugs Bureau of the DDF at the central level where all the information is consolidated and forwarded to the Central Medical Store (CMS). CMS also manages the storage and distribution of medicines. The procurement of essential medicines follows the treatment guidelines set by the national therapeutic committee and its expert sub-committees for specific diseases (including malaria). The supply chain of antimalarial medicines operates in parallel to the regular supply chain. Medicines are also distributed in public health facilities (such as health centers, hospitals or health posts), through community health workers including VMWs, and in private for-profit health facilities (including hospitals, cabinets and clinics).

Pre-marketing authorization and licensing

Registration of pharmaceuticals

Registration of pharmaceutical products falls under the 2007 Amendment and is dealt with by the Registration and Cosmetics Bureau of the DDF. Registration procedures should take up to three months for innovator products and six months for generic drugs. A fast-track registration scheme is available in since 2009. It is unclear however where ACTs subsidized by the Global Fund are eligible for fast-track registration.

Licensing of manufacturers

The guidelines for the licensing of manufacturers are outlined in the Amendment 2007. As most pharmaceutical products in Cambodia are imported from abroad, the Prakas on Procedures and Conditions of the Submission of the registration of Pharmaceutical Manufacturers from Overseas (2013) is of particular relevance. According to this Prakas, manufacturing permits are valid for five years. Article 8 states that this permit is revoked in the event that the manufacturer is "accused on drug quality" by a local or international regulatory authority. This clause however provides very little information on what constitutes a breach of 'drug quality'.

Licensing of importers and wholesalers

Most pharmaceuticals circulating in Cambodia are manufactured overseas, and for this reason, the licensing procedures for wholesalers and distributors (including importers and exporters) are also of crucial importance. Both the DDF's Narcotic and Pharmaceutical Trade Bureau and the MoC regulate the wholesale and distribution of pharmaceutical products. The 1996 Law and its 2007 Amendment stipulate that the distribution and wholesale of pharmaceuticals should be under the responsibility of a technical pharmacist of Khmer nationality and member to the Cambodian Pharmacist Council. Approval to import medicines are usually granted for 6 months and must be renewed thereafter. Whether these guidelines are implemented systematically in practice however is unknown.

Licensing of Pharmacies and drug outlets

The licensing of pharmacies and drug outlets is regulated by the 2007 Amendment and the (2009) Prakas on the Formalities and Conditions for Opening /Closing /Relocation of a Pharmaceutical Selling Establishment. There are three types of public sector pharmaceutical outlets in Cambodia including Pharmacies, Depot A an Depot B outlets. Each have different licensing requirements. For example, Pharmacies must be owned by a pharmacist while a Depot B can be set up by a retired midwife or nurse. Depot A and B outlets can be smaller in size than Pharmacy outlets. Owners of all three however must hold a membership from the Cambodian Pharmacist Council.

Post-marketing surveillance and quality control

Pharmacovigilance and product recall

The Amendment (2007) grants the MoH a mandate to recall batches in case of reported adverse drug reactions. Cambodia also has a dedicated Pharmacovigilance Centre since 2008 with a Medicines Safety Advisory Committee that meets regularly. Cambodia is also a member of WHO International Drug Monitoring Programme. The 2010 Medicines Policy calls for a strengthening of the pharmacovigilance activities in Cambodia and encourages health workers to report adverse drug reactions. There is no known mechanisms for patients or consumers to report adverse reactions, treatment failures themselves.

Regulatory inspections and enforcement

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Quality monitoring inspections fall under the authority of the Drug Regulation Bureau. Inspections for quality control are conducted by 'Control Agents' whose activities are regulated by the 2007 Amendment and most significantly, the Prakas (2011) on Roles and Responsibilities of Control Agents. Control agents have a wide scope of responsibilities ranging from enforcement of manufacturing regulation, import and export rules as well as the opening / closing of pharmacies. The role of control agents is decentralized and central level inspectors monitor the implementation of activities every trimester at the municipal and provincial levels. Control agents use pre-defined check-lists to conduct their inspection activities and there are clear reporting guidelines. Whether this occurs in practice however is unknown. The main functions of the medicines quality control laboratory of Cambodia (the National Health Product Quality Control Centre (NHQC)) include; testing pharmaceuticals, participating in registration activities, inspecting industry quality control laboratories and collaborating with inspectorate to test collected samples.

Beyond health law

The Law on The management of Quality and Safety of Products and Services (2000) also offers opportunities for sanctions against drug falsification and provides a larger scope to regulate against such "fraudulent" activity. Article 3 states that product information on ingredients, composition and usage needs to be available in Khmer on the packaging. This provides an opportunity to regulate against medicines deemed falsified and coming from abroad that do not possess the right labelling requirements. It also legislates against the production or storage of poor-quality products (articles 17 and 19) and addresses the sell/resale of machinery that could be used in drug falsification activates (article 20). The law concerns products that can cause "grave or imminent danger" to consumers (article 22) however, the penalties incurred here are lower for falsification from 5 -10 million riels in fine and up to one year in prison (Article 63). This law provides greater scope for regulating against pharmaceutical crime but evidence of its implementation for pharmaceutical products is scarce and the extent to which the penalties above have been applied in the past is unknown as respondents suggest, there is not written evidence of convictions to date.

Appendix 10 – Stakeholder map Cambodia

Stakeholder	Acronym	Type	Mandate	Description	Alliances
Department of Food and Drug	DDF	Government	Regulation of the supply chain of pharmaceutical products and devices	Operates under the MoH and acts as national medicines regulatory authority. Responsible for management of supply chain of essential medicines	IMC; MoH; CNM; WMWs; UNOPS; GF (Funding for AML sampling and quality control)
Inter-Ministerial Committee to Fight against Counterfeit & Substandard Medicines (IMC)	IMC	Government	Committee gathering cross-ministerial support for efforts against poor-quality medicines	Key mechanism against poor-quality medicines. Operates in decentralized manner with central, municipal and provicincial commissions with representatives from all ten ministries: the Ministry of Health, of Agriculture, of Commerce, of Defence, of Economy and Finance, of Education, of Forestry and Fisheries, of Information, of Interior, of Justice and the Ministry of Youth and Sport.	MoH; MoF; MoI; MoA; MoE; MoD; DDF

Ministry of Health	MoH	Government	Health service delivery in Cambodia	Ministry in charge of pharmaceuticals.	IMC; DDF; CNM; VMWs; WHO
National Centre for Entomology, Parasitology and Malaria Control	CNM	Government	Management of Malaria Control Program in Cambodia	Operates semi-indepdendently to MoH. Reports to Director of General health Services. Principal Reciptient of Global Fund grants for procurement of antimalarials until 2013.	UNOPS; CAP-M
Village Malaria Workers	VMWs	Government	Provides key human resources to improve acces to quality government AML treatments in rural areas of Cambodia. Conduct Rapid Diagnostic Tests (RDTs) and refer severe cases to hospitals. Keep records.	Introduced in 2011 by CNM and WHO Cambodia first piloted in Northeast and expanded gradually until 2008. Extension of public health service delivery arm of MoH.	MoH; CNM, CAP-M; GF (Funding)

World Health Organization Cambodia Office	WHO	International Organisation	Support health system improvement in Cambodia and improve quality of health services as a strategic priority including essential medicines and products.	Respondents confirmed the role of the WHO in highlighting the need to secure the supply chain of AMLs and strengthen the medicine regulatory system. The WHO acts as oordination hub for health-related activities in Cambodia. The WHO plays an important role here as a steering committee to align donor priorities to the needs of the country and promote the sustainability of those collaborative approaches. WHO is Lead Donor Facilitator of the Technical Working Group on Health to facilitate the relationship between the public and private sector and to facilitate governance and decentralization efforts (WHO, 2011).	MoH; BMGF; USAID (Funding); DFAT (Funding); GF (Funding)
Population Services International	PSI/PSK	Implementing Partner	Improve access to health services	International non-profit organization. Works with CNM and DDF to implement the Public Private Mix Strategy. Provides subsidized malaria commodities (Malarine and Malacheck) through private sector program since 2003. Runs quality assurance program verifying quality of antimalarials and prescription habits in private outlets	BMGF; ACTw; MC; CNM; DDF

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United Nations Office for Project Services	UNOPS	Implementing Partner	Efficient procurement and distribution of antimalarial treatments in Cambodia	Current Principal Recipient (PR) for Global Fund grant	GF (UNOPS is Principal Recipient); CNM; DDF
United States Pharmacopeia	USP	Implementing Partner	Improve standards for the quality of medicines by monitoring quality in 12 sentinnel sites with the use of the minilab, providing technical support for national laboratory and raising awareness about the quality of medicines.	Non-profit organization working with DDF since 2003 and funded predominantly throguh USAID's President Malaria Intiative. Runs the USP Promoting the Quality of Medicines Program in collaboration with DDF	USAID; DDF; MoH; CNM
Interpol	INT	International Organisation	Track and arrest criminal networks of poor-quality medicines in Southeast Asia	Since 2005 conducts yearly short-term operations with customs and police representatives in Southeast Asia including Cambodia to to disrupt transnational pharmaceutical crime networks by uncovering routes and handing those responsible to justice. Raise awareness through media about problem of poor-quality medicines.	MoI; MoH; POL; CUST;

ACT watch	ACTw	Non-governmental organisation	Research for malaria control, prevention and treatment	Multi-country project addressing gaps in evidence related to antimalarial medicines and case management. Also conducted surveys on private sector outlets and oAMT availability in Cambodia to inform policy	PSI/PSK
CAP-Malaria	CAP-M	Non-governmental organisation	Working for the prevention and control of Malaria in the Mekong Region	Oversees VMWs and works in collaboration with URC-C to reduce morbidity and mortality from malaria in the region of the Mekong. Also operates in Mynamar and Thailand.	USAID; URC-C; VMWs; DDF
Malaria Consortium	MC	Non-governmental organisation	Working for the prevention and control of Malaria in the Mekong Region	International non-profit organization in Cambodia since 2009 providing tehcnical support to government for malaria control efforts. Conducts operational research in rural areas. Not working on circulation of antimalarial treatments per se but indirectly supports access to good quality treatments	PSI; CNM; DDF
Medicam	MEDICAM	Non-governmental organisation	Upholding network of NGOs working on access to health in Cambodia	Non-governmental association for local organizations working in health - helps coordinate health projects across the sector	All NGOs

Univeristy Research Co Cambodia	URC-C	Non-governmental organisation	Improve equitable access to health care in Cambodia.	Improving health infomration management system and logistics information management systems.	USAID; CAM-M; VMWs; DDF
Bill and Melinda Gates Foundation	BMGF	Donor organisation	Supporting efforts for the prevention and control of Malaria	Funding for PSI activities to support access to affordable quality antimalarial treatments in the private sector.	PSI; WHO
Fonds de Solidarité Prioritaire Mekong (France)	FSP	Donor organisation	Financial support and diplomatic action to harness capacity against trafficking of poor-quality medicines	Project ended in 2015, mainly cooperating with Ministry of Defense to gather political support against the trade in poor-quality medicines in the Mekong region, including Cambodia.	MoI; MoD
Japanese Pharmaceutical Manufacturers Association	JPMA	Donor organisation	Support efforts to improve pharmaceutical regulation	Little information available.	MoH; DDF
The Global Fund to Fight Aids, Tuberculosis and Malaria	GF	Donor organisation	Supporting efforts for the prevention and control of Malaria since 2003	Round 9 of funding for the support of malaria control efforts 2010-2015. Country Coordinating Mechanism as a multi-stakeholder partnership with public and private representatives working on malaria, HIV AIDS and Tuberculosis.	UNOPS; VMWs; CNM

| United States Agency for International Development | USAID | Donor organisation | Working for the prevention and control of Malaria in the Mekong Region through the President's Malaria Initiative | Supports most implementing partner organisations in the fight against malaria, support capacity building efforts in particular. Works through USP, Cap Malaria in Cambodia. | USP; CAP-M; URC-C; WHO |

Appendix 11 – Document analysis Cambodia

Title	Type	Sector	Body	Date	Objective	Scope	Observation
Guidelines for the Regulatory Agency Department of Drugs and Food Cambodia	Official Guidelines	Government	Ministry of Health	2009	General guidelines on main activities of the DDF	Broad	General guidelines, relevant to understand functions of the DDF
Ministry of Health Procurement Guidelines for GFATM (version 8)	Official Guidelines	Government	Ministry of Health	2006	Management of procurement activities	Broad	General guidelines, relevant to understand procurement process
Royal Kram on Management of Pharmaceuticals	Law	Government	National Assembly of Cambodia	1996	Management of Pharmaceutical Sector	Targeted	First general law to deliniate the role of pharamcists and penalties incurred if rules are not respected.
Decision on Establishment of Committee for Eliminating Counterfeit Medicines, and	Decision	Government	Royal Government of Cambodia	2005	Inter-sectoral cooperation against counterfeit medicines	Targeted: dealing with counterfeit medicines specifically	Encourages cooperation across ministries. Cooepration decentralized in two separate commissions. Linked to the reduction of poverty.

Illegal Health Services for Poverty Reduction							
Pharmaceutical Products Recall Guideline	Official Guidelines	Government	Department of Drugs and Food, MoH Cambodia		Pharmacovigilance and product recall	Targeted: Pharmacovigilance and regulation against harmful and dangerous medicines	Recall procedure does not refer to terminology of falsified medicines but discusses pharmaceutical products that are dangerous to health and discusses what to do in case those are found.
Good Pharmacy Practices Guide	Official Guidelines	Government	Department of Drugs and Food, MoH Cambodia	2006	Guidelines for pharamacists	Targeted	Provides instructions on quality of pharmaceutical products on sale from labelling instructions to adequate warehousing and storage facilities. Alludes to how to deal with poor-quality products without providing specific definition. "spurious" or "expired" medicines – to be kept separately for destruction. It does not however define what constitutes a "spurious" medicine.

Law on the amendment of Law on Management of Pharmaceuticals	Amendment to Law	Government	National Assembly of Cambodia	2007	Management of Pharmaceutical Sector	Targeted	Revision of 1996 Law. Revision of penalties incurred for sale and import of poor-quality medicines at Articles 10-13
Health Strategy Plan 2008-2015	Plan	Government	Ministry of Health	2008	Strategy for improving health sector delivery (broad spectrum)	Broad spectrum, strategy fo improving health sector delivery	Strengthening health system at large.
The National Strategic Plan for Elimination of Malaria in the Kingdom of Cambodia 2011-2025	Report	Government	Royal Government of Cambodia	2011	Strategy for Malaria control and elimination	Broad spectrum, focus on malaria control and elimination.	Information on distribution of antimalarial commodities.

Medicines Policy	Policy	Government	Royal Government of Cambodia	2010	Strengthen pharmaceutical sector through development of appropriate legislation and regulation of medicines including quality control and registration procedures		Reinforces the Kram 1996 and amendment 2007. More of a strategic plan with a focus on improving quality control.
Law on The management of Quality and Safety of Products and Services	Law	Government	Royal Government of Cambodia	2000	Quality control for all goods and services.	Not pharma specific but on general management of quality of goods and services	Opportunities for sanctions against drug falsification activities. Larger scope to regulate against such fradulent activity. This law also encourages inter-ministerial cooperation. This law is not specific to pharamceutical products.

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Prakas On Procedures and Conditions of the Submission of the registration of Pharmaceutical Manufacturer from Oversea	Law	Government	Ministry of Health	2013	Registration of foreign manufactureres	selective - upstream available - production and manufacturing of medicines	Manufacturing permits are valid for five years. Article 8: permit is revoked in the event that "it is accused on drug quality from local and international competent authorities". This clause however provides very little information on what constitutes a breach of 'drug quality'.
Sub-Decree on the Orgnization and Functioning of the Ministry of Commerce	Law	Government	Royal Government of Cambodia	1997	Functions of the Ministry of Commerce	targeted : Focuses only on activities under the Ministry of Commerce	Interesting approach and departments for dealing with international porganizations an intellectual property.

Prakas on Roles and Responsibilities of Control Agent for Pharmaceutics, Foods, Medical equipment, and Comsmetics and Private Medical, Paramedical and Medical Aid Services	Law	Government	Ministry of Health	2011	Role of Control Agents in Cambodia.	targeted and comprehensive - specifically against counterfeit medicines and enforcement of the Law on Management of pharmaceuticals. Although it also includes Food and Hygiene.	Wide scope of responsibilities for control agents. Responsibilities includes Food and Hygiene, as well as Comestics. Decentralized approach to implementation and control activities.
Prakas on the Formalities and Conditions for Opening / Closure or Relocation of a Pharamceutical Selling Establishment	Law	Government	Ministry of Health	2009	Registration and administrative requirements for pharmceutical selling establishments	Targeted on pharmaceutical establishment and management of licensing and operations	There are three types of public sector pharmaceutical outlets in Cambodia including Pharmacies, Depot A an Depot B outlets.

Appendix 12 – Laos pharmaceutical regulatory system

Procurement of medicines

Medicines for the public sector are funded through the national budget. A tendering committee within the MPSC is responsible for the budget for the procurement of medicines registered in the Lao National Essential Medicines List (NEML). The MPSC only does the procurement for the national budget, not for the Global Fund (GF) and mainly procures medicines from local generic manufacturers (50-60%). The rest of the medicines are imported from abroad. Provincial officers are in charge of quantifying the needs and requirements per therapeutic category, with the help of the village and district level offices of the MoH. The budget of the Food and Drug Department relies on fees for the evaluation and registration of medicinal products, fees for the licensing of establishments as well as surveillance activities on request of the manufacturers. Funding from donor organization supplements the government budget.

Pre-marketing authorization and licensing

Registration of pharmaceuticals

The registration procedure for modern drugs is overseen by the Drug Registration Unit under the FDD's Drug Control Division and by a Drug Registration Committee of experts. Standard application forms are available through the FDD, first to submit a sample for verification and subsequently to apply for product registration. Both manufacturers and importers can submit applications. A decision is typically made within six months and is signed off by the Director of the FDD. Fees are incurred at various stages of the registration process as highlighted by section 5 of the Regulation Governing Drug registration (2003). The FDD decides which medicines to approve based on the current National Essential Medicines List. The 8th version of this the Lao NEML is available on the FDD website and uploaded in June 2016. The FDD is mandated by the NMP (2003) to publish a Food and Drug Bulletin to inform of registration decisions. The list of currently registered medicines (1,449) is available on the FDD website. Drug registration certificates are valid for three years and can be renewed subject to reapplication. There is no fast-track registration process available in Lao PDR, even for AMLs.

Licensing of manufacturers

The (2011) Amended Law on Drugs and the revised NMP (2003) currently regulate the licensing of manufacturers. Applications are reviewed and licenses granted by the licensing unit of the Drug Control Division of the FDD. There is a list of seven requirements that manufacturers must fulfil before being granted a license to manufacturer medicines (Law on Drugs 2011, article 14). For example, manufacturers are required to have at least five years of experience as pharmacists before applying for a license to manufacture. The applicant must have "appropriate premises, necessary facilities, standardized warehouse and transportation vehicles" as well as adequate safety and environment protection measures in place. Finally, a list of all licensed manufacturers, both domestic and international pharmacies for import purposes, is available in Lao on the FDD website.

Licensing of wholesalers and distributors

The conditions for the licensing of wholesalers and importers or distributors are the same, as listed in the Amended Law on Drugs (2011, article 14). Further requirements stipulated in the Law on Drugs state that wholesalers, distributors, and importers cannot be licensed if they hold a criminal record and must employ a pharmacist of Lao nationality. Pharmaceutical traders must also comply with legislations under the Ministry of Industry and Commerce, such as the Law on Enterprises and Labor Law, to conduct business in Laos. Prior to importing any pharmaceutical product, the importer must register the product with FDD. The MoH conducts sample tests upon the first import batch before issuance of an import certificate. Conditions on facilities meant for the import and export of medicines are detailed in the Provision 1442/MoH (2003, Article 4) and include guidelines on hygiene, restrictions on location, regulation on the use of special signage, and equipment requirements such as glass cabinets as well as an adequate warehousing system. For storage of imported medicines and medicines ready for distribution in Laos, four regional warehouses and one central warehouse in Vientiane were built with the support of the Japan International Cooperation Agency (Tabernero et al. 2015).

Licensing of pharmacies and drug outlets

All licenses are issued by the licensing division of the Drug Control Division at the FDD. According to the most recent information on the FDD website dating back to 2013, a total of 2,093 pharmacies are registered in Laos. The pharmacy license is valid for one year and needs to be renewed three months before expiration. The current legal framework prohibits pharmaceutical outlets from selling counterfeit, subs-standard, deteriorated or expires drugs, to participate in false advertising, or to assign any person not fully qualified to the dispensing

of medicines. Additionally, the Law on Health Care (2005, article 27) encourages the strict application of prescription requirements stating that "drugs shall be issued by pharmacists, nurses or midwives, who shall strictly comply with the prescriptions made by the physician or dentist and shall provide the patients with a detailed explanation of their use."

Post-marketing surveillance and quality control

Pharmacovigilance and product recall

The 2000 and 2011 Law on Drugs, as well as the 2003 NMP provide guidelines on pharmacovigilance activities and product recall. According to the 2003 NMP, products that have been proven unsafe or ineffective will be recalled. In accordance with the 2000 Law on Drugs, the MoH established a Toxicology Information Center mandated to disseminate information about drug toxicology, to issue recommendations in case of chemical toxicity, and to collect and disseminate information on Adverse Drug Reactions (ADR). Finally, according to the 2011 Amended Law on Drugs (Article 42) the MoH has the duty to handle propositions relating to drug quality standards.

Regulatory inspections and enforcement

According to the Amended Law on Drugs (2011) the organizations in charge of enforcing the above rules and regulations and conducting regulatory inspections include the FDD at the central level, as well as the Departments of Heath of Provinces, and District Health Offices. Since 2014 however, the BFDI conducts all inspections independently.

Beyond health law

Also of relevance is the revised Customs Law (2011) which does not specifically refer to poor-quality or 'fake' medicines, but refers to "Prohibited Goods" and "Controlled Goods" (at article 31). This law also stipulates measures to protect IP rights on the initiation of the trademark owner (Article 32) and outlines measures to prevent smuggling of illegal goods across the Mekong River (Article 71). Such guidelines are also relevant in the fight against the illegal circulation of poor-quality medicines. The customs law also offers the possibility to penalize importers for the smuggling in of illegal goods, which is considered here as a 'serious offense' and is punishable by a fine valued at 30%-50% of the total value of goods in fine (article 91). While article 95 of this law does not state that the owner of these illegal goods holds criminal responsibility in civil law, chapter 3 outlines strict procedures for the

submission of a case to court. The extent to which these provisions are enforced however is unknown.

Appendix 13 – Stakeholder map Laos

Stakeholder	Acronym	Type	Mandate	Description	Alliances
Ministry of Health	MoH	Government	Health service delivery in Laos	Principal Recipient of GF grant - through the Communicable Disease Control Department. Ministry in charge of regulating pharmaceuticals.	GF; FDD; BFDI; CMPE; MPSC; LOMWRU
Food and Drug Department	FDD	Government	Regulation of the supply chain of pharmaceutical products and devices.	Operates under the MoH and acts as national medicines regulatory authority. Responsible for management of supply chain of essential medicines from pre-marketing registration to post-marketing surveillance.	MoH; USP; BFDI; LOMWRU
Bureau of Food and Drug Inspection	BFDI	Government	In charge of drug quality control activities through the inspection of pharmaceutical outlets.	Operates under the MoH and as an independent quality control agency. Receives funding from the GF and technical support from USP. Meets occasionally with police, customs and trade authority. In charge of inspection activities.	GF; FDD; MoH; MoC; POL; CUST; LOMWRU
Medical Products Supply Center	MPSC	Government	Procurement of essential medicines in Laos.	Operates under the MoH and is the main procurement agent for essential medicines in Laos.	MoH; FDD

Centre for Malaria Parasitology and Entomology	CMPE	Government	Management of Malaria Control Program in Laos.	Operates semi-indepdendently to MoH. Reports to Director of General health Services. Trains VMWs for distribution of medicines and administering Rapid Diagnostic Testts,	MoH; VMWs; GF; LOMWRU
Village Malaria Workers	VMWs	Government	Provide human resources to improve acces to quality AMLs in rural areas of Cambodia.	Extension of public health service delivery arm of MoH. Conduct Rapid Diagnostic Tests (RDTs) and refer severe cases to hospitals. Keeps records.	MoH; CMPE
Customs	CUST	Government	Law enforcement of trade and import and export laws on all products including pharamceuticals.	Involved in anti-smuggling activities. Participates in INTERPOL Operations STORM.	BFDI; POL; INT;
Police	POL	Government	Law enforcement for pharmaceutical and trade laws	Participates in adhoc meetings with BFDI on quality control of pharmaceuticals and enforcement of licensing and registration requirements. Participates in INTERPOL Operations STORM.	BFDI; CUST; INT
United States Pharmacopeia	USP	Implementing Partner	Improve standards for the quality of medicines by monitoring quality in all provinces with the use of the minilab,	Non-profit organization working with FDD since 2003 and funded predominantly throguh USAID's President Malaria Intiative. Runs the USP Promoting the Quality of Medicines Program in collaboration with DDF.	FDD; MoH; BFDI; LOMWRU

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				providing technical support for sampling and testint activites.	Main implementing partner for technical capacity support.	
World Health Organization Lao PDR Office	WHO	International Organisation	Support health system improvement in Laos.		Supports the establishment of Standard Operating Procedures for pharmaceutical sector, and Good Manufacturing Practice. Also supports efforts to promote the rational use of medicines in Laos.	MoH
ACT watch	ACTw	Non-governmental organisation	Research for malaria control, prevention and treatment.		Multi-country project addressing gaps in evidence related to the supply of antimalarial medicines and case management in Southeast Asia. First survey conducted in 2015 in Laos.	PSI; MoH
Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit	LOMWRU	Non-governmental organisation	Building evidence base for prevalence of poor-quality including falsified and substandard medicines in Laos since 2000.		Research on medicine quality epidemiology in Laos and in Southeast Asia. Participates in the Worldwide Antimalarial Resistance Network.	FDD; BFDI; MoH; CMPE; USP
Swedish International Development Cooperation Agency	SIDA	International Organisation	Support regulatory framework for management of pharmaceuticals		Supported MoH and FDD in the drafting of first National Medicines Policy in 1993 and establishing first drug quality control center. Phased out in 2008.	MoH; FDD

The Global Fund to Fight Aids, Tuberculosis and Malaria	GF	Donor Organisation	Prevention and control of Malaria.	Main donor to malaria programme in Laos. Budget (5 million US$) to train inspectors at detecting poor-quaity antimalarial medicines.	MoH; CMPE
United States Agency for International Development	USAID	Donor Organisation	Prevention and control of Malaria in the Mekong Region through the President's Malaria Initiative.	Supports USP PQM Activities in Laos, PSI and ACTw surveying activities.	USP; PSI; ACTw;
Asian Development Bank	ADB	Donor Organisation	Improve health care in Southeast Asia to support economic and social development in the region.	Supports national malaria programme in 12 provinces by expanding malaria surveillance systems. Working with MoH.	MoH
World Bank	WB	Donor Organisation	Promote growth for economic and social development. Supports the development of the health sector.	Promotes social development by supporting efforts to improve maternal and child health, and nutrion. Also supports health services implementation to increase utilization of public health service and improve the quality of the servics offered.	MoH

Appendix 14 – Document analysis Laos

Title	Type	Sector	Body	Date	Objective	Scope	Observations
National Medicine Policy	Policy	Government	Food and Drug Department, MoH	1993	Policy aimed at strenghtening equitable access to quality, safe and efficacious medicines, and improving their rational use.	Targeted	Drafted with international partners including SIDA, and approved in 1993. reviewed in 2003 (see below). New NMP is now the main reference policy.
Revised National Medicine Policy	Policy	Government	Food and Drug Department, MoH	2003	Policy aimed at strenghtening equitable access to quality, safe and efficacious medicines, and improving their rational use.	Targeted	(Section 8) on quality assurance of medicines. Pokicy calls for more data to guide policy making.Pharmacovigilance: Products that have been proven unsafe or ineffective will be recalled. (Article 1.4) encourages cross-sectoral cooperation, especially with law enforcement agencies; "FDD will cooperate closely with other law enforcement agencies in enforcing this legislation".

Law on Drugs and Medical Products 01/NA	Law	Government	National Assembly	2000	Outlines general principles of drug management and ensure registration, distribution, and supply of quality medicines.	Targeted	Outlines registration procedures through the FDD drug registration units under the Drug Control Division and with the help of a Drug Registration Committee of experts. Law revised in 2011 which is now the main reference law.
Amended Law on Drugs and Medical Products 07/NA	Law	Government	National Assembly	2011	Outline general principles of drug management and ensure registration, distribution, and supply of quality medicines.	Targeted	(Article 14) Sets conditions for licensing of businesses involved in the production, distirbution, wholesale, import/export of pharmaceutical prodcuts - list of 7 requirements. (Article 39.3) Prohibitions on 'business operators' to sell drugs that are 'counterfeit, substandard, deteriorated or expired'. (Article 47) Efforts to enforce rules and regulations are rewarded: "Individual, legal entities or organizations with outstanding achievements in implementing of this Law, such as: business operation of drugs and medical products with good quality; manufacturers, companies and model pharmacies shall receive rewards and other policies in accordance with the laws and regulations." (Article 52) on pharmacovigilance states that the MoH has the duty to handle propositions relating to quality and standards of the drugs. in terms

						of post-marketing surveillance this law states that the FDD is responsible for inspections. Since 2014 however the BFDI is the main inspections agency. This would need to be reviewed in subsequent laws.
Law on Health Care	Law	Government	National Assembly	2005	Outlines the rules that regulate health services and the health sector at large.	Broad	(Article 27) Enforces the prescription of drugs. (Article 62) Efforts to promote the implementation of this law are rewarded. This is intented to encourage effective implementation of the law throughout the health sector.
Regulation 1441/MOH Governing Drug Registration	Law	Government	Ministry of Health	2003	Outlining rules and regulations with regards to the registration of modern and traditional medicines in Laos.	Targeted: Pre-marketing authorizat ion only	Highlights procedure to apply for a marketing aurhotization for medicines. Document states that there should be an annual audit on the procurement of pharmaceuticals conducted by the Laos Ministry of Finance. Document plans incremental penaltis for individuals or businesses who sell 'counterfeit' or 'unregistered' medicines include: First violation: warning and confiscation; Second violation: fine at 100% of total value and temporary closure of 1 year. Third violation: fine at 200% and permanent closure of facility.

Provision 1442/MOH On the establishment of drug and medical equipment import-export companies	Law	Government	Ministry of Health	2003	Outlines rules and regulations pertaining to the import and export of pharmaceutical products in laos.	Targeted	Stipulates measures against importers who do not respect the current regulations. On the case of smuggling, importing or exporting bad quality, banned or counterfeit drugs. First violation: warning and a fine at 200% of the price of all goods. Secnd violation: fine at 400% and temporary closure for one year. Third violation: afine at 600%, permanent closure and case sent to court.
Revised Customs Law 04/NA	Law	Government	National Assembly	2011	Outlines principles, policies, rules and measures on export-import, transit and movement of goods within Lao PDR.	Broad: Focus on customs control	Focused on supporting the country's social and economic development by strengthening reuglating on the import/export of all products. Law includes guidelines on customs declarations, statements on origin or valuation of products etc. (Article 32) on the protection against IP infringement. (Article 56) states that goods obtained through donations or grant aid are exempt from customs duties. (Article 31) Refers to 'Controlled Goods' and 'Restricted Goods' the latter category does not include falsified medicines 'Controlled Goods' likely to encompass pharmaceuticals for which other state authorities (i.e. the FDD) are also involved in the regulating their circulation. (Article 71) on the prevention of smuggling

						across the Mekong river, boats must be registered with customs authorities.
Law on Making Legislation	Law	Government	National Assembly	2012	Guidelines to ensure the transparent development and amendment of legislation across sectors in Laos.	Broad	Encourages transparent revision of current laws. Aims to support regional harmonisation of regulatory frameworks, wherever possible.

Appendix 15 – Thailand pharmaceutical regulatory system

Procurement of medicines

The 1967 Drug Act divides medicines in different categories: household drugs, dangerous drugs (prescription-only drugs such as hyper-tension drugs or antibiotics), specially-controlled drugs (costly medicines such as anti-cancer drugs or corticosteroid) and non-dangerous. The category determines how these medicines are distributed. In line with this categorization, pharmacies are divided into those allowed to sell prescription-only drugs where a pharmacist is present at all times, and those for over-the-counter drugs only (Holloway 2012). The price of medicines is determined in collaboration with the Ministry of Commerce (Teerawattananon et al. 2003). The procurement of medicines is organized by province; hospitals join into this system to negotiate cheaper prices.

The TFDA today operates with 96 members of staff centrally and up to 500 members of staff across its provincial divisions. While the main laws and regulations emanate from the central TFDA, the implementation of these laws is the responsibility of PPHOs. The TFDA regulates a sector of over 17,000 drug stores, wholesalers and distributors, approximately 150 manufacturers and about 30,000 pharmaceutical products (Holloway 2012).

The National Drug Committee, now known as the NDSDC was first set up in 1991 with 14 members appointed by the Minister of Public Health every two years since then. This committee meets on a monthly basis to discuss registration approvals, withdrawals and suspension of licenses. This committee appoints six subcommittees overseeing more specific activities such as the review of applications for registration, the establishment of GMP requirements, or licensing approvals for manufacturers, importers, distributors or drug stores.

Pre-marketing authorization and licensing

Registration of Pharmaceuticals

Applications for drug registration are submitted to the Drug Control Division of the TFDA. Processing of registration procedures is divided between the central office and the PPHOs. There are two different application processes; one for generic and another for New Original Drugs. First an application is made to submit a drug sample for quality testing. This can take up to two weeks. For generic drugs, the application is followed by an application to the TFDA

for a Certificate of Drug Quality & Standard Control Method. Samples are transferred to the Medical Sciences Department's Drug Analysis Division before approval can be issued. For New Original drugs, application procedures follow the ACTR and ACTD format for innovator drugs. Standard review for a new drug takes between 210 and 280 days. There is a fast track process for both new and generic drugs lasting approximately 100-130 and 70 days respectively. A number of essential medicines including antimalarial treatments are eligible for fast track marketing authorisation. A list of approved medicines is communicated regularly and updated every 3 to 6 months (Cite CoRE).

Licensing of manufacturers

Manufacturers within Bangkok submit an application for a license to manufacture medicines to the central TFDA's Drug Control Division directly. For manufacturers based in any other province, application are submitted to the relevant PPHOs. A license to manufacture medicines is only granted to Thai citizens or Thai enterprises. Another condition is for at least 2 pharmacists to be employed and at least one to be on duty during all business hours. Drug Act 1967 (Section 38) details the role of the pharmacist in 6 parts. Before granting a license to manufacture, the TFDA inspects the premises to assess compliance with Thai Good Manufacturing Practices (GMP) Guidelines. Drug Act 1967 (section 25) encourages manufacturers to arrange for an analysis of the raw materials used in the production of the drugs, with evidence of such analyses kept for at least 5 years. Once issued, the manufacturing license is valid for one year. This license can be revoked if the manufacturer is found in breach of the Drug Act.

Licensing of importers and wholesalers

Applications for a license to import are submitted to the Drug Control Division of the TFDA for businesses operating in Bangkok and its adjacent territories. Licensing procedures beyond the Bangkok province are delegated to the PPHOs as above. The application requires clinical trial reports and a Marketing Authorization from the country of origin. If the application is successful, importers receive an Importer Authorization License after which, the company needs to send samples for registration of the product to the TFDA. A successful product registration thereby acts as a license to import. This license is valid for one year. A pharmaceutical company that is licensed to import or to manufacture drugs is also licensed to wholesale. Again, a pharmacist needs to be present at all times during business hours of the wholesale enterprise. Section 26 of the Drug Act 1967 also regulates the export of medicines.

Licensing of pharmacies and drug outlets

Licenses to sell medicines are issued by the TFDA and are valid for 1 year. These are subject to renewal each year although the business can continue operating as long as the application for renewal has been submitted. With the exception of special-controlled drugs which require a prescription for sale, all other medicines are sold over-the-counter. Pharmacies that can sell special-controlled drugs however are obliged by law to have a pharmacist present on the premises during all business hours. One respondent adds that Good Pharmacy Practice guidelines are now in place and require all drug stores to have a pharmacist present on the premises at all times of business. Drug Act 1967 (Section 39) details the role of the pharmacist at points of sale in 6 parts. Finally, according to section 33 of the Drug Act 1987 amendment, all licensed outlets should have qualified staff present during business hours. 33bis calls of a replacement of staff in case of long absences. For all licensing procedures detailed in this section, section 18 of the Drug Act 1967 allows for the applicant to appeal to the licensing authorities within thirty days of receiving a notice, in case of a negative answer.

Post-marketing surveillance and control

Pharmacovigilance and product recall

Aside from the 2-year safety-monitoring program, during which all medical professionals are encouraged to report ADRs or concerns regarding the quality and safety of a pharmaceutical under temporary registration to the TFDA, there is a dedicated center for pharmacovigilance activities in Thailand with its own separate budget; the National Centre for Pharmacovigilance (NHPCV) since 1983. The NHPCV is a member of the WHO International Drug Monitoring Program since 1984 (Nwokike et al. 2013). In case of serious safety concerns, the products are sent for re-evaluation leading to the possible withdrawal of its marketing authorization and to product recalls. During the application for marketing authorizations all pharmaceutical companies submit a 'recall commitment' document guaranteeing that they will abide by the recall procedures if triggered to do so by the TFDA. All serious ADRs must be reported within 24 hours. Unexpected ADRs can be reported within 7 days and can take up to 60 days for non-serous ADRs (Nwokike et al. 2013). By encouraging the registration of drug formulae by producers or importers, section 79 of the Drug Act 1967 lays the ground work for the development of a Thai Pharmacopeia. Regulatory inspections and enforcement.

The TFDA is keen on consumer education and regularly shares information about adverse drug reactions or poor-quality medicines via its website. Section 76 of the 1967 Drug Act empowers

the Minister to issue a Government Gazette with information on pharmacopeia. The TFDA has previously issued information leaflets and conducted information campaigns on these priority topics.

Regulatory inspections and enforcement

TFDA inspectors conducting post-marketing surveillance activities are pharmacists by training or scientists with relevant technical expertise. They follow pre-determined standard operating procedures to conduct these inspections. These inspectors are mandated to conduct sample testing on the spot through portable test-kits or to select samples to be sent for laboratory analysis at the Medical Sciences Department. The NDSDC appoints a sub-committee to evaluate the quality of registered products. Inspectors within this sub-committee are mandated by the Drug Act 1967 to enter premises to inspect outlets, factories, wholesale enterprises, or storage facilities and evaluate their compliance with existing legislation. TFDA inspectors have the authority to sample products, seize goods if those are suspected of being of poor-quality as well as to imitative product recalls.

Penalties

as stipulated in the Drug Act 1967, violations of the rules and regulations are penalized by a combination of monetary fines and imprisonment. Section 72 explains that it is forbidden to produce, sell or import. The production of fake drugs is liable to 3 years to life in prison, and to a fine of 10,000 – 50,000 baht (section 117). The production of substandard or unregistered medicines is liable to 2-5 years in prison and a fine of 4,000 to 20,000 baht (Section 118). Penalties for selling and importing a fake medicine is 1 to 20 years imprisonment and a fine of 2,000 to 10,000 baht (Section 119). The penalty for selling or importing a substandard or unregistered medicine is 6 months to 3 years and 1,000 to 5,000 baht (section 120). There are also penalties for selling or importing deteriorated drugs at up to a year in prison and up to 3,000 baht (Section 121).

Beyond Health Law

There are malaria sections in 12 Offices of Disease Prevention and Control at the regional level, 39 Vector-Borne Disease Centers (VBDCs) at the provincial level, and 302 Vector-Borne Disease Units (VBDUs) at the district level (BVBD 2011). At the sub-district level, the program delivers diagnostic and treatment services through 650 Malaria Clinics, as reported in 2009 (Thumm 2009).

Appendix 16 – Stakeholder map Thailand

Stakeholder	Acronym	Type	Mandate	Description	Alliances
Ministry of Public Health	MoPH	Government	Health service delivery in Thailand.	Main health authority responsible for formulating and implementing health policy. Ministry in charge of regulation of pharmaceuticals.	TFDA; DCD; DMS; VHVs; NHSO; MoIT; Mo
Drug Committee	DC	Government	Control of pharmaceutical products.	Advising Minister of Public Health on regulatory and technical aspects of administration and control of pharmaceutical products. Provides guidance on national policies for regulation of pharmaceuticals. Appointed by the Cabinet every two years with new members, approximately forteen. Authorised to approve/withdraw pharmaceutical registrations and licenses.	MoPH; TFDA
Thaid Food and Drug Administration	TFDA	Government	Protection of consumer health and ensuring the safety, quality and efficacy of health products.	Acts as drug regulatory authority of Thailand. Established in 1974 and restructured in 2003. Now operates under the MoPH as a department. Responsible for management of supply chain of all medicines.	MoPH; DCD; GPO; USP; CHULA; POL

Drug Control Division	DCD	Government	Under the TFDA, this is the devision responsible for pre- and post-marketing activities related to medicines.	In charge of the pre- and post-marketing control activities for medicines, as well as the general administration and development or revision of policies. Main focus is on infectious diseases.	TFDA; DMS
Department of Disease Control	DDC	Government	Sets standards and guidelines to address main disease threats in Thailand; including Malaria.	Hosts the Malaria Control Program under the BVBD. Develops laws and policies to combat key priority diseases and implements those through a network of 12 regional offices of and provincial offices	MoPH; BVBD
Bureau of Vector Borne Diseases	BVBD	Government	Under the DDDC, hosts malaria program.	Repsonsible for all vector-borne diseases, including malaria. Operates the surveillance system, oubtreak control, and developmentof pilot programs. Working through Provincial Public Health Offics as well. Operates under the Department of Disease Control and works in collaboration with the BDN for quality control.	MoPH; DDC; BDN; GF; USP
Department of Medical Sciences	DMS	Government	Oversees laboratory services for public health institutions.	Improves standards for the quality of medicines by monitoring quality. Supports policy development for post-marketing surveillance in Thailand.	MoPH; TFDA; BDN; BLQS

Bureau of Drugs and Narcotics	BDN	Government	Medicine surveillance.	Works in coperation with Thai FDA for enforcement of drug quality controls. Testing of medicines. Integral part of post-marketing sureillance activities of TFDA. Works with BVBD on tesitng the quality of AMLs. Also cooperation with USP. Confirmatory testing laboratory in the region with USP - tests samples from Cambodia, Laos, Vietnam for confirmatory tests. Total number of staff is 137, including 68 pharmacists, 14 scientists, and 12 laboratory assistants. BDN samples approximately 2,500 drugs annually.	MoPH; TFDA; BVBD; USP; GF
Bureau of Laboratory Quality Standards	BLQS	Government	Testing quality of pharmaceutical samples.	Works under the DMS and the BDN to provide technical expertise in testing the quality of sampled medicines. An essential player in post-marketing surveillance activities of the TFDA.	DMS; BDN; TFDA; BVBD
Government Pharmaceutical Organization	GPO	Government/ Industry	Supply of locally produced quality generic medicines including antimalarial medicines and other essential drugs.	State entreprise that produces and supplies medicines for the Thai government and directly to public hospitals. Also manages stocks of medicines. Main procurer of locally produced generic medicines in Thailand.	MoPH; TFDA

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Village Health Volunteers	VHVs	Government	Provides key human resources to improve acces to health services and medicines at the village level in Thailand.	Extension of public health service delivery arm of MoPH. Participate in basic drug quality testing for essential medicines through visual (paper) tests.	MoPH; BDN
National Health Security Office	NHSO	Government	Financing of medicines in Thailand.	Responsible for the budget for drugs and vaccines under the Universal Health Coverage Scheme (formerly known as the 30 Baht scheme) which covers 74% of the population.	MoPH; TFDA
Royal Thai Customs	CUST	Law Enforcement	Law enforcement of trade and import/export laws on medicinal products.	Law enforcement to prevent smuggling of illegal goods through active border control, including pharamceuticals. Participates in INTERPOL Operations STORM. Cooperates with Thai FDA at the border with presence of health inspectors.	TFDA; MoPH; UNODC; INTERPOL; POL; MoC; MoI
Royal Thai Police	POL	Law Enforcement	Law enforcement for pharmaceutical and trade laws.	Responsible for law enforcement of licensing requirements in pharmacies. Main division is the Consumper Protection Division (CPD) and the Information Technology Division (ITD) dealing with internet pharmacies. Participates in INTERPOL Operations STORM.	TFDA; MoPH; INTERPOl; CUST; MoC; MoI

United National Industrial Development Organization	UNIDO	Implementing Partner	Support in establishment laboratory facilities for drug testing.	Provided support to Chulalongkorn University while setting up a quality control laboratory and prto improve laboratory capacity in neighbouring countries such as Myanmar.	CHULA; MoPH
United Nations Office for Drugs and Crime	UNODC	Implementing Partner	Capacity building to improve customs control against 'fraudulent' medicines.	Works in collaboration with Royal Thai Customs and builds capacity (programme management, evlaluation) through the Conainer Control Program (CCP) since 2004. CCP is operated with the World Customs Organization. Supports STORM operations.	CUST; WCO; INTERPOL
United States Pharmacopeia	USP	Implementing Partner	Improve standards for the quality of medicines by monitoring quality. Supportpolicy development for post-marketing surveillance in Thailand.	Non-profit organization working with TFDA and Chulalongkorn university. Funded predominantly by USAID's President Malaria Intiative. Runs the USP Promoting the Quality of Medicines Program.	TFDA; CHULA; BDN; DMS
Management Sciences for Health	MSH	International Organisation	Research on supply chain of pharmaceuticals and quality control.	Worked with Chulalongkorn on a survey evaluating the pharmceutical supply chain in Thailand as well as in other countries of Southeast Asia.	CHULA; MoPH

Chulalongkorn University	CHULA	Non-governmental organisation/ Academia	Research for improving pharmaceutical regulation.	Collaborates with USP since 2008 for medicine quality control in Thaialnd. Conducts training on anaysis of antimalarial medicines. Also trains neighboring countries and their laboratory staff in medicine quality testing, through trainer-the-trainor programmes.	TFDA; MoPH; MSH; USP; UNIDO;
Pharmaceutical systems research and development doundation	PhaRed	Non-governmental organisation	Working to improve access to medicines.	Provides medicine information on online database for free in Thai. Supports basic access to 'household medicines' in schools.	MoPH; TFDA
PReMA	PReMA	Industry	Association of pharmaceutical manufacturers in Thailand.	Bangkok-based industry association representing the pharamceutical industry in negotiations towards policy-making with the MoPH and the TFDA. Involved in the discusisons towards the draft new Drug Act (2006). Raises awareness among manufacturers of the dangers of poor-quality medicines.	MoPH; TFDA
World Health Organization	WHO	International Organisation	Working with BVBD on resistance to artemisinin issues.	Supports MoPH in coordination of Malaria Programm and in efforst against other diseases. Supports efforts against the rising resistance to artemisinin at the Thai-Cambodian border.	BVBD; DDC; MoPH
The Global Fund to Fight Aids,	GF	Donor organisation	Supporting efforts for the prevention and control of	Fund efforts for malaria control, and not for malaria elimination since 2004 in Thailand (since Round 2). Provides funding for procurement of AMLs.	BVBD; DDC; MoPH

Tuberculosis and Malaria			Malaria since 2003.		
United States Agency for International Development	USAID	Donor organisation	Working for the prevention and control of Malaria in the Mekong Region through the President's Malaria Initiative.	Finances the main activities of USP in Thailand.	USP; TFDA; MoPH

Appendix 17 – Document analysis Thailand

Title	Type	Sector	Body	Date	Objective	Scope	Observation
Drug Act	Law	Government	Ministry of Public Health	1967	Comprehensive law outlining general guidelines on main activities of the TFDA and MoPH.	Broad	27 pages of rules and regulations outlining functions of the TFDA. From registration procedures, licensing requirements, manufacturing requirements, the role of pharmacists in all licensed outlets, and penalties incurred if clauses of the Drug Act are not respected. Medicines are divided in four categories: household drugs, dangerous drugs, specially-controlled drugs and non-dangerous drugs. The Drug Act also outlines the role of TFDA inspectors and their mandate while conducting inspections on licensed outlets and products on sale. Section 79 lays the ground for the development of a Thai pharmacopeia by encouraging all domestic drug manufacturers to register their drug formulae. Chapter 8 of the Drug Act outlines rules and regulations pertaining to fake, substandard, deteriorated and unregistered medicines.

Drug Act Amendment	Law	Government	Ministry of Public Health	1987	Amendments to Drug Act 1967 per seciton.	Broad	Latest revisions to general guidelines stipulated in Drug Act 1967. Section 27bis calls for the insepction of modern drugs (imported) at all ports of entry into Thailand. Section 33 states that all licensed outlets should have qualified pharmacists present during business hours. Section 38 proposes a differentiation between fake drugs that are "harmful" to consumers and those that are not. This differentiation is dangerous and hard to implement in practice.
National Health Security Act	Law	Government	Ministry of Public Health	2002	Improving access to health services for all.	Broad	Reshapes the health financing system of the MoPH to sustain Universal Health Coverage.
New Drug Act (draft)	Law	Government	Ministry of Public Health	2003	Revision of Drug Act 1967 and Amendments. New guidelines on main activities of the TFDA and MoPH and pharmaceutical regulation in Thailand.	Broad	Still in promulgation stage and currently being debated at the National Assembly. Suggests revision to existing Drug Act. For example the New Drug Act is said to reinforce GMP compliance for issuing manufacturing licenses within Thailand. It also plans to tighten the rules on dispensing of medicines. The New Drug Act also plans to implement a product liability mechanism whereby consumers will be able to sue drug manufacturers if the medicine causes harm. The New Drug Act proposes to review the current penalties for the production, distribution and sale of fake, substandard, deteriorated and unregistered medicines.

National Health Act	Law	Government	Ministry of Public Health	2007	Strategic guidelines for the developemnt of the health sector in Thailand.	Broad	Focused on notion of developing general "well-being" in Thailand. Stronger focus on preventive medicine and other alternative medicines.
National Drug Policy (2012-2016)	Policy	Government	Ministry of Public Health	2011	Guidelines on access to medicines and rational use of medicines.	Targeted	Goal is to promote "universal access to medicines for all, rational use of medicines and national self-reliance". Policy developed by the National Drug System Development Committee and introduced alongside the National Strategic Action Plan 2012-2016. Promotes access to medicines and rational use of medicines by providing further guidelines to strengthen the regulatory system in order to ensure quality, efficacy and safety or registered medicines. Promotes the development of the domestic pharmaceutical industry.
National Strategic Plan for Malaria Control and Elimination (2011-2016)	Guidel ine	Government	Ministry of Public Health	2011	Guidelines for the implementation of malaria control programme through the Bureau of	Targeted	One of the main objectives of this plan is to "ensure access for all to early diagnosis and affordable, safe, effective and prompt antimalarial combination treatments through active public and private sector initiative".

					Vector Borne Diseases.		
11th National Health Development Plan (2012-2016)	Guideline	Government	Ministry of Public Health	2012	General strategy for the development of the Thai health sector and pharmaceutical indsutry.	Broad	Highlights health priorities for Thailand between 2012-2016, mentions the need to strengthen the services provided by sub-district health promoting hospitals in order to support the decentralization of the health sector.