The Problem of Substandard Medicines in Developing Countries

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Foreword

The La Follette School of Public Affairs at the University of Wisconsin–Madison offers a two-year graduate program leading to a Master of Public Affairs or a Master of International Public Affairs degree. In both programs, students develop analytic tools with which to assess policy responses to issues, evaluate implications of policies for efficiency and equity, and interpret and present data relevant to policy considerations.

Students in the Master of International Public Affairs program produced this report. The students are enrolled in the Workshop in International Public Affairs, the capstone course in their graduate program. The workshop challenges the students to improve their analytical skills by applying them to an issue with a substantial international component and to contribute useful knowledge and recommendations to their client. It provides them with practical experience applying the tools of analysis acquired during three semesters of prior coursework to actual problems clients face in the public, non-governmental, and private sectors. Students work in teams to produce carefully crafted policy reports that meet high professional standards. The reports are research-based, analytical, evaluative, and (where relevant) prescriptive responses for real-world clients. This culminating experience is the ideal equivalent of the thesis for the La Follette School degrees in public affairs. While the acquisition of a set of analytical skills is important, it is no substitute for learning by doing.

The opinions and judgments presented in the report do not represent the views, official or unofficial, of the La Follette School or of the client for which the report was prepared.

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Executive Summary

In this report we undertake an investigation of substandard medicines and the threat they pose to global treatment programs. Even licensed manufacturers produce substandard medicines and fail to meet basic quality control tests. At best, these medicines are ineffective; at worst, they create drug-resistant pathogens or result in death. We frame the problem of the spread of substandard medicines as two-fold: market failure and government failure. Misaligned incentives cause both problems. Significant government and international intervention is therefore justified to address the problem.

Our goal in this report is to map the environment in which substandard medicines are produced, regulated, and distributed, drawing on examples from relevant actors. Specifically, we focus on five international organizations, six countries, and two groups of manufacturers that we selected after reviewing the literature. Our analysis indicates that the prevalence of substandard medicines results from problems along the supply chain including improper quantification, procurement, storage, distribution, and use of medicines.

Our recommendations address three broad policy goals: to align incentives across the medical supply chain; to improve overall supply chain management; and to clarify the definition of and increase the international emphasis on substandard medicines. We offer practical suggestions for meeting these goals.

A Note on Methodology

To describe the environment in which substandard medicines proliferate, we first reviewed literature on the nature and extent of the problem. We then reviewed studies concerning the proliferation of substandards in the developing world. We sorted the studies into three types: large studies, which tested medicines in more than five countries; medium-sized studies, which tested medicines in two to five countries; and single-country studies (see section 2.3).

In the core of our report (section 4) we examined case studies of three major actors along the medicine supply chain: manufacturers, international organizations, and national governments. We matched information from two sources (the list of Fortune 500 pharmaceutical companies and a list of manufacturers known to make substandards). We examined two types of manufacturers: the large multinational Novartis and smaller firms in Vietnam.

For international organizations, we focused on international organizations that contribute significant financial amounts to supplying medicines in developing countries. We then discussed seven organizations, dividing them into those that provide long-term health care (the World Health Organization, UN Development Programme, UN Population Fund, UN Children's Fund) and those involved in disaster and relief work (International Red Cross and Red Crescent Movement,

International Federation of Red Cross and Red Crescent Societies, and Médecins Sans Frontières).

Finally, we presented case studies of six countries that are significant exporters and importers of substandard medicines. These countries illustrate the diverse causes of the spread of substandard medicines and the range of responses adopted to address the problem. For exporter countries we investigated China, India, and Thailand; for importer countries we investigated Nigeria, Ghana, and Kenya.

These case studies informed our understanding of the problem and our final recommendations. A more detailed explanation of our methodology can be found in each section.

1. Introduction

Substandard medicines pose a serious public health risk, especially in the developing world. Produced by licensed manufacturers, these medicines are the product of poor manufacturing practices or improper storage or distribution practices, that result in deterioration in the quality of the medicines (World Health Organization n.d.a). Substandard medicines run the gamut from products that contain correct ingredients in incorrect proportions to products without active ingredients or with harmful substitutes (World Health Organization 2010b).

At their very best, these medicines are ineffective; at worst, they cause harm, creating drug-resistant pathogens or resulting in death. Substandard antimalarials in Africa, for example, engender drug resistance by exposing parasites to sub-lethal concentrations of active ingredients (Newton et al. 2011). Substandard medicines also pose a political risk, as they erode public confidence in health delivery systems (World Health Organization 2010b).

Although substandard medicines proliferate in international medical supply chains, efforts to control them vary widely across countries. Medical regulatory legislation differs from country to country, and implementation of legislation depends on national regulatory and enforcement agencies (World Health Organization n.d.a). Because medical supply chains cross borders frequently, weaknesses in regulatory or enforcement mechanisms in a single country can corrupt the entire supply chain.

In this report, we frame the issue of substandard medicines as problems of market failure and government failure, both caused by misaligned incentives. We then map out the environment within which medical supply chains operate, with a focus on the primary manufacturers, wholesalers, transporters, retailers, and consumers of substandard medicines. For manufacturers, we focus on pharmaceutical companies that tend to produce substandard medicines and the countries in which they operate. For consumers, we investigate international organizations that purchase medicines for humanitarian purposes and the countries where substandard medicines are distributed.

The report is structured as follows. Section 2 lays out the problem of the proliferation of substandard medicines, discussing the differences between substandard and counterfeit medicines, the harmful effects of such medicines, and the extent of the problem. In this section, we also frame the problem as misaligned incentives that lead to market and government failures . Section 3 describes the medical supply chain, the important actors along the chain and their significance, and the problems they face in regulating medicines. In Section 4, the core of the report, we describe regulations and safeguards at each level of the supply chain and analyze case studies that exemplify the range of problems. Section 5 outlines our recommendations for limiting the spread of substandard medicines.

2. Defining the Problem

The spread of substandard medicines is attributable to a number of factors. These include weak supply chains, failed distribution networks, an abundance of small-scale suppliers, lack of integration of regulatory actors, poor information technology systems, and limited financial resources. In this section, we distinguish between substandard and counterfeit medicines, outline the harmful effects of substandard medicines, discuss the extent of their propagation, and frame the problem of the spread of substandards as market and government failures caused by misaligned incentives.

2.1. Difference between Substandard and Counterfeit Medicines

This report focuses on substandard as opposed to counterfeit medicines. Substandard medicines are made by licensed manufacturers operating within the framework of national pharmaceutical regulatory standards. Also referred to as "out of specification" products, these include medicines sold past their expiration date, medicines that have been compromised in shipping or storage, and medicines that are missing active ingredients or contain the wrong ratio of active ingredients (World Health Organization n.d.c). Substandard medicines may arise due to human error, negligence, or resource restrictions (World Health Organization 2003). They may result from both inadvertent and deliberate actions by a legitimate manufacturer.

Caudron et al. (2008) identify ten categories of substandard medicines: over-concentration of active ingredient, under-concentration of active ingredient, irregular filling of vials, contamination, mislabeling (not counterfeit), problems with active ingredient, problems with excipients (inactive ingredients used as carriers for active ingredients in medicines), poor stability, packing problems, and unsatisfactory dissolution profiles. These categories exemplify the diverse number of ways medicines may be rendered substandard.

By contrast, counterfeit medicines, defined by the World Health Organization (WHO) as "spurious/falsely-labeled/falsified/counterfeit" medicines, are "deliberately and fraudulently mislabeled with respect to identity and/or source" (World Health Organization 2010b). Although substandard and counterfeit medicines are similar in that both have serious public health implications, counterfeits are not produced by licensed manufacturers. Although counterfeits tend to be substandard (in that they do not contain correct amounts of active ingredient), this is not inherent in the definition of counterfeits.

The difference in manufacturers means the problems with substandard and counterfeit medicines are distinct. Substandard medicines, for example, can be controlled through effective regulation and enforcement, because manufacturers are known and licensed. Counterfeits, however, can be produced in homes, small industries, and backyards, and are harder to regulate (International Medical Products Anti-Counterfeiting Taskforce 2008).

In this report, we focus on substandard medicines as defined above. However, because substandard medicines are not always separable from well-made counterfeits, some discussion will necessarily include mention of counterfeits.

One reason coordination of medical regulations tends to be difficult across countries is that each country adopts its own definitions of substandard and counterfeit medicines. India, for example, distinguishes between "spurious" and "grossly substandard" medicines but does not differentiate by manufacturer (Central Drug Standard Control Organization of India n.d.b). Although the WHO distinguishes between substandard and counterfeit medicines, member states have not universally adopted these distinctions (World Health Organization 2011).

Finally, it should also be noted that "generic" medicines, that is, medicines produced without patent protections, are inherently neither substandard nor counterfeit, so we do not specifically address them.

2.2. Harmful Effects of Substandard Medicines

Medicines may be rendered substandard at any point along the medical supply chain, from the point of manufacture through the point of distribution. At manufacture, medicines may be produced with impure or improper proportions of active ingredients. But even if produced properly, medicines may be compromised during transportation, warehousing, distribution, or even as a result of improper storage by the consumer.

Regardless of where along the supply chain substandard medicines are compromised, they pose serious public health risks. Use of substandard medicines increases mortality and morbidity and may result in harmful side effects or allergies or engender drug-resistant pathogens that limit the therapeutic effectiveness of legitimate medicines (Newton et al. 2011; Newton et al. 2010; Nsimba 2008; Hogerzeil et al. 1992). Substandard medicines also contribute to the spread of infectious diseases (Nsimba 2008) and, if contaminated with pathogens (fungi, bacteria, viruses, or parasites) or other toxic elements, can cause further illness or poisoning (Bate 2012b).

At worst, substandard medicines result in death (Caudron et al. 2008; O'Brien et al. 1998; Aldhous 2005). For example, contaminated paracetamol cough syrup resulted in 89 deaths in Haiti in 1995 and 30 infant deaths in India in 1998. The WHO also estimates that "of the one million deaths that occur from malaria annually, as many as 200,000 would be avoidable if the medicines available were effective, of good quality and used correctly" (World Health Organization 2003).

Substandard medicines also have social and economic effects, as they may reduce patients' confidence in their doctors, pharmacists, and even in modern medicines as a whole (Nsimba 2008). Patients who consume substandard medicines also suffer economic losses, as they spend income on ineffective medication. In the developing world, where medicines can constitute a substantial percentage of

individual income, such economic losses may be significant. Illness and death affect individual income and national economies, as they result in loss of productive worker time. Furthermore, since the use of substandard medicines often leads to illness, additional costs for health-care workers are incurred. The need to guard against substandards also results in costs for regulatory agencies and enforcement authorities (Newton et al. 2010). These additional health-care and regulatory costs include personnel costs for health-care workers and regulatory and enforcement agents, equipment costs for medical equipment and drug testing laboratories, and administrative costs.

Finally, the spread of substandard medicines has political ramifications (World Health Organization 2010b). Substandard medicines undermine governments' investments in health delivery systems. They erode citizens' trust in their governments' ability to maintain and enforce regulatory standards. Their spread also undermines governments' credibility with respect to providing quality health care.

2.3. Extent of the Problem

Substandard medicines are present throughout the global supply chain; in developing countries, the problem is acute. The WHO estimates that up to 25 percent of medicines consumed in developing countries are substandard (World Health Organization 2003).[1] According to the WHO, 30 percent of countries have either "no drug regulation, or a capacity that hardly functions" (Newton et al. 2011, 18). Even in places where national medicine distribution channels have been created to ensure drug quality and safety, those channels have proven incapable of eliminating the problem of substandard medicines (World Health Organization 1999). This problem is further confounded by the Internet, where "illegal sites that conceal their physical address" may sell counterfeit medicines (World Health Organization 2010b).

A case in Bangladesh in the early 1990s exemplifies the difficulty in detecting the source of substandard medicines, monitoring the drug supply chain, and enforcing pharmaceutical legislation in a developing country. At some point along the supply chain, foreign or local manufacturers, importers, or local distributors substituted diethylene glycol for the more expensive propylene glycol. This drug appeared in the Bangladesh hospital, Dhaka Shishu, and resulted in an outbreak of diethylene glycol poisoning, which continued for almost three years. When ingested, diethylene glycol causes fatal renal failure. The culprit was never identified, but after the contaminated drug was detected, renal failure in the

[1] This high percentage compares to isolated cases in the United States, where concern over substandards relates to high imports of medicines and active ingredients from developing countries. By its own account, the U.S. Food and Drug Administration (FDA) is not able to fully regulate pharmaceutical imports (U.S. Food and Drug Administration n.d.). Recent and ongoing studies by the Institute of Medicine analyze the FDA's and international actors' potential for addressing shortfalls in regulations and safeguards against substandard medicines internationally (Riviere and Buckley 2012; Institute of Medicine n.d.).

Bangladesh hospital decreased by 54 percent (Hanif et al. 1995). These medicines may have originated from the legitimate manufacturer, or they may have been counterfeit medicines.

Substandard medicines often do not pass even the most basic quality control tests, but data related to their propagation are scarce (Shakoor et al. 1997, 839). Although many studies run quality control tests on samples of medicines, reporting on the detected proportion of substandard medicines, they do not all follow the same standards. Some studies, for example, use the terms counterfeit and substandard interchangeably. Few studies analyze the prevalence of substandard medicines alone, and many studies focus only on the quality of antimalarial, tuberculosis, and antibacterial medicines. Sample size varies greatly and studies sometimes reach contradictory results. Literature on the assessment of counterfeit and substandard medicines quality is vast; in this section we outline a few recently published sources.

We were unable to find systematic information regarding the global prevalence of substandard medicines, so we reviewed individual reports on medicines quality tests. Working within our time constraints, we examined the reports as we found them, using common search terms. Although we do not believe that studies testing medicines in many countries necessarily employ more rigorous research methods than single-country studies, multicountry studies arguably offer more consistent comparisons across countries. We organized information into three groups: large studies, which test medicines in more than five countries; medium-sized studies, which test medicines in two to five countries; and single-country studies. We located fewer large and medium-sized studies than single-country studies. A table outlining findings of all 33 studies we examined is attached as Appendix A.

Large studies indicate that Nigeria and Ghana consistently have the highest rates of substandard medicines. Kenya, Cameroon, Mali, Zimbabwe, Sudan, Mozambique, and Gabon also show high rates of substandard medicines in at least one large study. Medium-sized studies find high levels of substandard medicines among Indian exports to Africa and in Kenya, Ghana, Uganda, and Nigeria. Single-country studies confirm the above findings for Nigeria, Kenya, and Indian exports. Single-country studies also find high rates of substandard medicines in Laos, Thailand, China (by some estimates), Bangladesh, Tanzania, and Cambodia.

2.4. Substandard Medicines as Market and Government Failures

We frame the problem of the proliferation of substandard medicines as a two-fold: market and government failure. At the core of both these issues is a misalignment of incentives.

Medicines are post-experience goods, meaning that consumers may not be able to perceive the quality of the product even after consuming it. Consumers have difficulty isolating the effects of the product because they cannot compare the

observed outcome to the counterfactual, namely the outcomes using different treatments on an identical patient, under identical circumstances. Markets for post-experience goods are particularly prone to failures related to information asymmetry. More specifically, producers and consumers have access to different degrees of information about the product, which leads to inefficient market outcomes (Weimer and Vining 2011, 105-106).

In this case, inefficient market outcomes occur when people consume substandard medicines because they lack sufficient information about the quality of the medicine. If they had complete information about the product, they would consume the optimal amount (in the case of substandard medicines, the optimum is usually none); because people lack information, they consume beyond the optimal amount. As discussed above, this overconsumption endangers their immediate health and causes significant secondary effects: decreased productivity and, in the case of contagious diseases, a public health hazard.

While procurers and consumers of medicines have an incentive to buy and consume high-quality products, producers have an incentive to maximize profits. For many goods, consumers can perceive the quality of a good and will only buy when quality is satisfactory. In that case, producers will cut costs only to the point where they can still produce a product that will sell. However, when consumers cannot perceive product quality, low-quality goods sell equally well as high-quality, so producers respond to the incentive to cut costs and maximize profits. This situation is called a market failure because the unregulated market leads to a suboptimal outcome.

The fact that individual decisions to consume medicines affect public health represents an additional form of market failure: a negative externality. Although the wider public does not participate in individual choices to consume, it is affected by those choices. Illness and disease impose health-care and economic costs on society. The negative externalities associated with consumption of substandard medicines magnify the urgency of the problem.

Governments generally respond to the classic market failure of information asymmetry by creating and enforcing regulations. These regulations serve to provide missing information directly (by requiring that drug companies provide information about potential side effects and contraindications, for example) or indirectly (by granting and withholding approval of a medicine, signaling to consumers whether the medicine meets a basic safety standard). Ideally, these services simplify consumer choices and give consumers the information they need to adjust consumption levels to the optimal amount. In practice, national regulatory agencies often do not have the funding, expertise, and processes in place needed to fulfill this role (Caudron et al. 2008, 1-2)

The large quantity of substandard medicines that reaches consumers is due to a series of government failures at several stages. First and foremost, national governments often lack incentives to devote sufficient resources to regulate and

monitor the medicines market. In the case of exports, if procurers and consumers continue to purchase medicines from manufacturers regardless of the risks, governments have little incentive to regulate the production of medicines. India and China, for example, are some of the largest producers of substandard medicines, but they are also some of the largest exporters of medicines in the developing world. In the case of imports and domestically produced medicines, if consumers are unable to force governments to regulate medicines (which happens in cases when consumers lack awareness or political power, as is common in many developing countries), governments will not commit the resources necessary to regulate effectively (Médecins Sans Frontières 2011, 1-2).

Second, many countries lack regulatory frameworks that sufficiently outline regulations or punishments for breaching regulations (Caudron et al. 2008, 1-2). Additionally, many countries do not have processes in place to monitor and regulate the supply chain. As supply chains cross borders, effective regulation requires coordination among national regulatory authorities, police, customs services, and national judiciaries. The market for medicines is thoroughly internationalized, and no government has proven capable of perfectly regulating the medicines produced or sold within its borders. Addressing these problems requires international cooperation among national governments and international organizations (World Health Organization 2003).

Last, regulatory bodies may not succeed at safeguarding the public because of bureaucratic failures, funding problems, and difficulty gaining top expertise in a field where producers stand to gain more than regulators (Caudron et al. 2008, 1-2). Bureaucratic failure leads to decreased efficiency as a result of agency loss,[2] limited competition, expensive civil service protections, and difficulty in assessing achievement in terms of monetary value (Weimer and Vining 2011, 178-185).

3. Actors along the Supply Chain

The medicine distribution chain can be visualized as a pyramid with fewer suppliers at the top than at the bottom (i.e., there are a few wholesale centers, but the distribution network is vast) (Patouillard et al. 2010, 3). Medicines are not shipped directly from the manufacturer to the consumer, but pass through wholesalers and retailers before reaching the consumer (Dutton 2004). At each level, problems may harm the quality of the medicine, leading to substandard medicines.

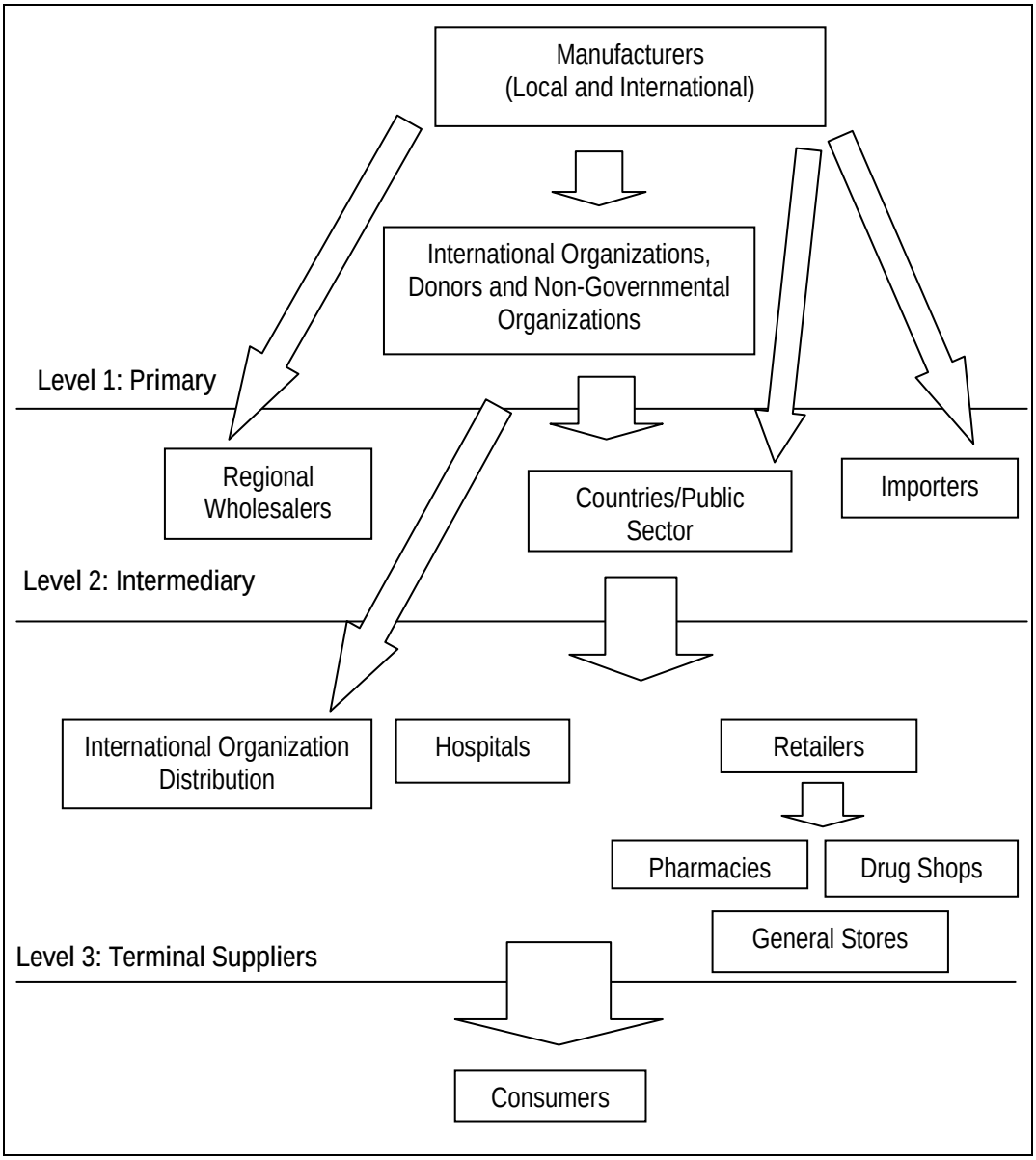
[2] Agency loss refers to lawmakers' delegation of some decision-making power to bureaucratic agencies. These agencies usually do not function in perfect alignment with lawmakers because their incentives do not perfectly match lawmakers' incentives. Lawmakers may attempt to minimize agency loss by enhancing accountability through submission of reports on activities (Lupia 2001, 3-6).

Lessons can be learned from studies that compare and contrast the medical supply chains with other mass retail supply chains. According to Agwunobi and London (2009, 1336), mass retailers in non-health industries have reduced costs and improved quality by eliminating middlemen, purchasing in bulk, and embracing price competition. Adopting similar efficiency improvements would increase the quality, reach, and affordability of medicines.

However, the ways in which medical supply chains differ from other consumer product supply chains makes adoption of certain improvements more difficult. First, the production of genuine medication is highly capital intensive and skill intensive. Readily available monetary resources and technical expertise to ensure a high-quality medicine supply chain vary from country to country. Second, medicines require a high degree of traceability, security, and monitoring. However, medical supply chains in the developing world lack systematic tools for information gathering. Third, unlike other consumer goods, which can leave a market if contracts are not complied with or enforced, medicines do not have that option. Fourth, medical production and consumption is governed by strict regulation in most countries, presenting challenges for international aid organizations, which must account for these different regulations. Deliveries might be delayed while aid organizations work with the host government to register a specific drug. Finally, given the length and complexity of the consumer chain and the small number of producers as compared to distributors, medicine manufacturers are limited in their ability to create incentives for other actors in the supply chain (Yadav et al. 2010).

Figure 1 illustrates the global supply chain of medicines in developing countries. It is followed by an introduction to each seven key actors along the supply chain. The seven are manufacturers, international organizations, national governments, wholesalers, transporters, retailers, and consumers.

Figure 1: Flowchart of Medical Supply Chain



Sources: Authors. Based on data from Patouillard et al. (2010).

3.1. Manufacturers

Pharmaceutical manufacturing is a complex industry that can be divided into five main categories: research and development-based multinationals, generic manufacturers on the international market, local companies based in a single country, contract manufacturers without their own portfolio, and biotech companies. The pharmaceutical industry is primarily made up of two production stages: one for active ingredient production, another for formulation and packaging. Active ingredients are produced in low amounts and at a few centralized locations because of their high value. Medicines and non-active ingredients used to produce them are manufactured by thousands of companies all over the world (Sousa et al. 2011, 2396-2399).

The pharmaceutical industry is vulnerable to substandard quality. Manufacturers depend on the quality of chemicals supplied to them, and substandard chemicals can compromise even the best-made medicines. The global reach of the manufacturing industry means that many countries do not have direct control over the manufacturing process until medicines reach their borders (World Health Organization 2003). Relative to value, medicines are very small, so a large amount of space and resources is not typically required to make them when they are poorly made. High-quality medicines, particularly medicines for the treatment of malaria, HIV, and tuberculosis, can be very expensive, even in generic form. Producers can make a large profit on medicines by simply reducing the amount of active ingredient mixed in each batch, which is a deliberate attempt to make medicine substandard (Wertheimer and Norris 2005, 4-16).

3.2. International Organizations

International organizations are among the main funders of medicines as humanitarian aid. They help to oversee medicine delivery in emergency situations and collaborate with other organizations to obtain donations of medicines. In addition to purchasing and providing essential medicines, international organizations propose solutions, analyze problems within the medicine supply chain, and develop methods of collaboration among different actors.

Although international organizations acknowledge the problem of substandard medicines and regularly emphasize their commitment to reducing the prevalence of substandard medicines, substandards continue to propagate in medical supply chains. International organizations are limited in their ability to regulate the spread of substandard drugs because most regulation and enforcement is done at the national level.

3.3. National Governments

Access to basic health care regardless of socioeconomic status is recognized internationally as a fundamental human right, as stated in the UN Universal Declaration of Human Rights, Article 25 (1948). Obtaining medicines that reach a standard of safety and quality is a necessary part of health care. As discussed in section 2.4, the free market does not reliably supply safe medicines, so governments must regulate medicine supply. This regulation is primarily carried out by national governments, which must develop comprehensive systems to guarantee safe and constant drug supplies.

National medicines policies combine many functions into single comprehensive regulatory systems. These functions include control of clinical trials; product registration; regulation of advertising; post-sale quality monitoring; and licensing and inspection of manufacturers, importers, exporters, wholesalers, distributors, pharmacies, and retail outlets (World Health Organization 2010a, 6).

Implementation and enforcement of an effective national medicines policy is a challenge for developing countries, where the problem of substandard medicines is greatest. Many factors complicate the problem at each stage of the supply chain: limited economic resources to procure medicines, let alone implement a national medicines policy; high burden of illness; limited pharmaceutical manufacturing capacity; diverse pharmaceutical supply chains; parallel counterfeit supply chains; logistical difficulties in safe storage, transport, and distribution; insufficiently trained personnel; uninformed distributors and consumers (World Health Organization 2010a, 4-6); and lack of economic resources and accessible channels of recourse for consumers (Médecins Sans Frontières 2011, 1-2). Developing countries also vary greatly in their capacity to manage comprehensive and effective regulatory systems for medicines. This variation results from differences in political incentives, funding, disease burdens, and a host of other factors (World Health Organization 2010a, 6).

3.4. Wholesalers

Wholesalers are key actors along the medical supply chain. They influence the chain in two important ways: by improving price and accessibility, and by influencing the behavior of other market participants. Regarding the first point, the non-governmental organizations, which often serve as wholesalers, have a relatively low monetary incentive to reduce quality and increase the price, because there are no shareholders demanding increased payouts. Evidence from Asia and the United States suggests that non-commercial suppliers influence commercial suppliers to improve the quality of products (Mackintosh et al. 2011, 2). This type of competition helps shape incentives and the market outcome for goods.

Since governments as well as international emergency relief agencies procure medicines directly from wholesalers, quality assurance at the wholesale level is

imperative. Quality control efforts by wholesalers vary greatly. For example, non-profit wholesaler International Dispensary Association delivers "high-quality essential medicines and medical supplies at the lowest possible price to low- and medium-income countries" (International Dispensary Association Foundation n.d.). Some countries, such as Tanzania, rely on the International Dispensary Association's quality assurance for testing their essential medicines. As of 2006, the association had tested batches of medicines made in the Netherlands, despite an expensive process (Mackintosh et al. 2011, 5). In comparison, wholesalers such as the Community Development Medical Unit based in India have pursued cost-cutting at the expense of quality assurance (Mackintosh et al. 2011, 2).

3.5. Transporters

Transport allows medicines to reach recipient countries and consumers along the medical supply chain. Problems, however, arise during transport that reduce the quality and potency of the drugs. In 1987, the United Nations International Children's Education Fund (UNICEF) sent $30 million worth of essential drugs to tropical countries. Hot and humid climates in these countries posed serious problems, with at least three medicines showing decreased concentrations of the active ingredient upon testing (Hogerzeil et al. 1992, 211). Transportation conditions, therefore, must be regulated and monitored.

3.6. Retail Suppliers

While retail availability, prices, and quality are partly dependent on suppliers further up the chain, the last link, medicine retailers (which include pharmacies, drug shops, grocery stores, market stalls, and itinerant hawkers) provide essential information regarding medicine intake to customers (Patouillard et al. 2010, 2). Problems at the retail supply level include: retailer lack of knowledge about the medicines they handle, stocking of unregistered medicines, and expiration of medicines (Patouillard et al. 2010, 8).

A study conducted in Laos on the knowledge and perception of medicines quality among sellers and consumers concluded that sellers lacked adequate scientific knowledge. The study tested knowledge of medicine quality using four criteria: correct labeling, testing, registration of medicines, and knowledge of active ingredients noted on the label. Of 59 sellers interviewed, only one had full knowledge of what determines a high-quality medicine. Fifty-one percent of urban sellers, 53 percent of rural sellers, and 39 percent of remote sellers could identify at least two of the four criteria (Syhakhang et al. 2004, 394).

A second problem relates to the stocking and selling of unregistered or illegal medicines. Outlets authorized only to sell over-the-counter medicines often illegally stock prescription medicines. For example, in Tanzania, stocking of prescription medicines without a permit is the norm. Additionally, while medicines sold in shops should be packaged and labeled, they are sometimes sold loose as individual tablets. Loose tablets of painkillers and antimalarial medicines were

found in 29 and 22 drug stores respectively, often packaged in homemade envelopes labeled with a hand-written note (Goodman et al. 2007, 397-398).

The expiration of medicines is a recurring weakness in the supply chain. Expiration may result from problems with medicine selection, quantification, procurement, storage, distribution, or use. Expiration of medicines is usually due to the slow turnover of expensive medicines and medicines that treat rare diseases, medicines with an unpleasant taste, donated medicines, and medicines affected by abrupt cessation as result of use or treatment policy changes (Nakyanzi et al. 2010, 154-155). Bulk purchasing, often done by international organizations, can lead to overstocking. Additionally, the complexity, inefficiencies, and lack of large-scale distribution networks in medicine supply chains contribute to the presence of expired medicines. As noted, sellers lack essential knowledge about labeling, testing, and registering drugs (Syhakhang et al. 2004, 393).

3.7. Consumers

Consumers are the last level along the supply chain; they purchase medicines directly from the retailers. As with medicine sellers, many consumers are unaware of the prevalence of poor quality in medicines. The Laos study concluded that 73 percent of consumers were unconcerned about the quality of the drugs they purchased. Additionally, 80 percent of urban consumers and 96 percent of rural customers were unaware that some medicines could contain less than the labeled amount of active ingredients. Consumers in urban areas were generally more aware of important criteria used to determine drug quality (Syhakhang et al. 2004, 391-396).

4. Regulations and Safeguards

This section outlines regulations (rules prescribed by authorities such as regulatory agencies) and safeguards (measures taken to ensure safety) and analyzes the effectiveness of regulations at various levels of the supply chain. Specifically, for each major actor in the supply chain (manufacturers, international organizations, and national governments), we identify weaknesses in the regulatory system or the safeguards, evaluate efforts to address those weaknesses, and propose policy solutions that address the source of the problem. We use case studies to inform our analysis for each major actor.

4.1. Manufacturers

Manufacturer data are difficult to find because analyses of medicine samples from around the globe generally do not identify the manufacturer of the medicine, but they identify the source country. We wanted to study two types of manufacturers. First, we wanted to look into large multinational manufacturers mainly from Europe and North America to see to what extent these manufacturers have problems with substandards or ingredient suppliers. Second, we wanted to look into small manufacturers from developing countries where substandard medicines

are produced. We used two separate approaches to determine which manufacturers to examine. First, we identified the largest global manufacturers using the *Fortune Magazine's* 2009 Top 500 Global Companies list (CNN Money 2009). We used the Fortune 500 list to identify manufacturers with the largest market share and the largest global presence (see Table C1 for a complete list). Second, we utilized the U.S. Pharmacopeial Convention's "Medicines Quality Database" to identify manufacturers, both large and small that had samples test as substandard. (For more information on the U.S. Pharmacopeial Convention, see Appendix B.)

For large multinational pharmaceutical companies, we wanted to discover how they could play a large role in substandard medicine prevention. We took a two-tiered approach to manufacturers from the Fortune 500 list. First, we checked the manufacturers from the list against medicines registered with the WHO Prequalification of Medicines Program. Ten companies from the Fortune 500 list have registered products on the WHO Prequalification of Medicines Program: Pfizer, GlaxoSmithKline, Novartis, Roche Group, Sanofl-Aventis, Pfizer, Abbott Laboratories, Merck, Wyeth (now part of Pfizer), and Bristol-Myers Squibb (World Health Organization n.d.b).

Second, we checked to see if any of the manufacturers from the Fortune 500 list appeared in any failed samples from the Medicines Quality Database because the database is the most comprehensive collection of medicine samples from countries that have problems with substandard medicine. Only one manufacturer, Novartis, had a failed sample (U.S. Pharmacopeial Convention n.d.). We chose to look at Novartis in further detail. Although Novartis has a failed sample on the Medicines Quality Database, we found it to be an example of a manufacturer that practices good supply chain monitoring and has high medicine production standards.

To study the problems of substandard medicine from small manufacturers, we analyzed the information obtained from the Medicines Quality Database, which provides the name of the manufacturer of the failed samples. We used the Internet to find the country of origin for each of the manufactures on the list. We decided not to include manufacturers of medicines from which fewer than five samples were taken. From the country matches we were able to obtain, the countries that have manufacturers with substandard samples are China, Guyana, Kenya, India, Thailand, and Vietnam. Of these countries, Vietnam had the largest number of manufacturers with failed samples. We therefore decided to conduct further research into the manufacturers in Vietnam. We would like to note that although these manufacturers were chosen based on failed samples, the Medicines Quality Database does not indicate where along the supply chain the medicine became substandard; however, the database was the best starting point for manufacturer research.

4.1.1. General Manufacturer Information

In addition to the two case studies, we wanted to provide additional information on manufacturers in general and what regulations and safeguards are in place to prevent substandard medicines.

We surveyed websites of pharmaceutical manufacturers from the Fortune 500 list to review standards and practices. We looked at counterfeit medicine response as well, since many manufacturers treat them as one issue and not two separate issues. We wanted to see how each of the largest manufacturers publicly acknowledges its role in the prevention of substandard medicines. Manufacturers vary in how they respond to substandard and counterfeit medicines. A review of each company website shows different levels of acknowledgement of substandard medicines as a problem, and support for both substandard and counterfeit prevention. Several companies reported supply chain inspections, rules for third party vendors, and other quality control measures throughout the production process. Some manufacturers have no website information on substandard medicines but mention counterfeit. (A summary of information availability from company websites is listed in Appendix C.)

Information on manufacturers' approaches to substandard medicines is more difficult to ascertain outside of the major multinational producers. Smaller manufacturers appear on a majority of failed samples from the Medicines Quality Database (see Appendix B). Manufacturers with failed samples often do not have any information on the Internet, other than address and phone listings within online country directories. Some evidence suggests that small manufacturers on the WHO Prequalified Medicines list have fewer problems with substandard medicines. We cross checked manufacturers listed there that had failed samples against the WHO Prequalified Medicines List. Two out of the 49 manufacturers have medicines on the prequalified medicines list: Cipla Ltd., and Ajanta Pharma Ltd., both from India (World Health Organization n.d.b; Table C1).

Pharmaceutical companies are key actors in minimizing safeguard weaknesses and strengthening the supply chain of medicines to developing countries. A study of the U.S. drug supply chain by the Pew Charitable Trusts ultimately came to this conclusion. The study made two recommendations. One of the recommendations is applicable at an international level: pharmaceutical companies must have comprehensive systems to ensure quality and safety, and security of drug distribution (Paris 2011). Pharmaceutical companies should acquire greater responsibility for the entire supply chain by increasing and improving oversight of manufacturers from which they purchase ingredients. They should require documentation of incoming drug ingredients. As medicines pass through the various stages in the medicine supply chain, numerous opportunities exist for products to be mishandled. To help mitigate these problems, increased transparency and oversight at every level is essential.

Pharmaceutical manufacturers will need increased pressure from national governments and international organizations to develop and enforce supply chain monitoring and safe practices. National governments can increase registration requirements and pass laws to hold manufacturers accountable for substandard medicines. International organizations can increase supply chain inspections or require use of the WHO prequalification program prior to the purchase of medicines from specific manufacturers.

4.1.2. Novartis

We initially selected Novartis because it has a substandard sample on the Medicines Quality Database and is the only large manufacturer on that list. However, this database only indicates that a sample procured at the consumer level is substandard and does not show where along the supply chain the product became compromised. According to the Medicines Quality Database, surveys of the antimalarial drug Coartem procured from Ghana and Kenya in 2010 show that one sample out of 106 was found to be substandard (U.S. Pharmacopeial Convention n.d.). Indeed, upon further research into Novartis's manufacturer standards and supply chain monitoring for their anti-malaria medicines, we found that Novartis is a manufacturer that should be emulated and serves as a good example of how a large pharmaceutical manufacturer can monitor all aspects of the supply chain and deliver medicine to a population most in need.

Novartis is a large, publicly held, multinational pharmaceutical company based in Basel, Switzerland. Novartis develops a wide range of medicines but it is a major producer of artimisinin-based combination therapy or ACT medicines to treat malaria. Since 2001, Novartis has sold more than 400 million doses of ACT medicines at cost to countries with endemic malaria. The main ACT medicine produced by Novartis, Coartem, is used primarily in the treatment of "uncomplicated" malaria (Novartis n.d.). Novartis's ACT medicines are listed on the World Health Organization Prequalified Medicines List (World Health Organization n.d.b).

Novartis takes a very hands-on approach through the entire process of the creation of ACT medicines from the cultivation of the sweet wormwood plant (where the active ingredient artimisinin comes from), all the way through delivery and distribution at the clinic level. Novartis provides investment, education, and technical support for its suppliers located in China. Suppliers are required to meet national and global regulatory standards. Active ingredients are then shipped to the United States for final manufacturing and packaging. The final product is stored in Switzerland until it is distributed to one of more than 60 countries (Novartis n.d.).

Novartis has built a large public-private partnership through its fight against malaria. It benefits from accountability standards set by shareholders and the public at large and from large profits gained from other medicines and patents. There is little evidence to suggest Novartis needs to change any policies or

methods in which it delivers high quality antimalarial medicine. Given the appropriate incentives, it is possible for other manufacturers to adopt similar supply chain standards and monitoring practices.

4.1.3. Manufacturers from Vietnam

Because individual manufacturer information from countries such as Vietnam was difficult to obtain, we looked into manufacturers as a whole from problem countries. According to our analysis of the Medicines Quality Database, almost one-third of Asian manufacturers with substandard samples are located in Vietnam (Table B1, Appendix B). Vietnam has taken some steps to reduce the number of substandard medicines produced there, but failed samples from the Medicines Quality Database show that substandard medicines are still a problem for these manufacturers.

Manufacturers from Vietnam are both state-owned (such as National Pharmaceutical Company No. 3 and National Pharmaceutical Joint-Stock No. 2) and privately owned (such as Nam Ha Pharmaceutical Joint-Stock Co. and Mekophar Chemical Pharmaceutical Joint-Stock Co.). The Medicines Quality Database shows that when analyzing Vietnam manufacturers who had at least five products sampled found 1-17 percent of medicines were substandard. This range is quite wide when compared to the percentage of substandard and counterfeit medicines in Vietnam during the early 1990s, which was around 8-9 percent. The reasons for this difference are the 15-20 percent annual growth rate of the Vietnamese pharmaceutical industry between 2000 and 2010 and the transition of the pharmaceutical industry from state monopoly to a competitive market in the last two decades. With a lack of government regulation on quality control, substandard medicine manufacturing increased because private companies sought higher profits from sales of low-price medicine rather than focusing on the production of high-quality medicine (SaVipharm n.d.).

To address the problem of substandard medicines that occurs during the manufacturing process, the Vietnamese government implemented a policy that forced every local drug manufacturer to meet the WHO's Good Manufacturing Practice (GMP) standards by 2008. The percentage of local manufacturers who met GMP standard increased from about 10 percent in 2006 to more than 50 percent in 2010 (Uki-Eagleton 2011; FDA News 2009). As of November 2011, Vietnam had 108 pharmaceutical factories that meet the WHO's GMP standard. Because GMP is the practice that helps to ensure the product's quality in the manufacturing process, any manufacturer that follows the GMP standard will produce fewer substandard medicines. Indeed, the most recent statistic shows that less than 3 percent of medicines in Vietnam in 2010 were found to be substandard (SaVipharm n.d.)

Although the GMP standard has helped to alleviate some of the problems of substandard medicines in Vietnam, manufacturers there continue to have a problem with packaging materials produced by manufacturers that do not meet

the WHO's GMP standard (SaVipharm n.d.) Unqualified packaging can fail to protect the medicine it contains, especially when exposed to the sunlight or harsh weather. To lower the risk of high-quality medicines becoming substandard because of low-quality packaging, Vietnamese manufacturers should use GMP-approved packaging.

The WHO's GMP standards are a good baseline for any national government to follow. In the case of Vietnam, follow-up research on medicines produced there is necessary to ensure that the national government has improved regulation and manufacturers do indeed produce less substandard medicine.

4.2. International Organizations

A large number of international organizations of various sizes provide medicines to developing countries. The exact roles of these organizations may be bewildering even to professionals in the field (International Medical Veritas Association n.d.). We have divided international organizations into two categories: long-term health-care or medicine providers and organizations specializing in emergency relief due. Long-term health-care or medicine providers consistently work with the same programs and generally purchase from the same manufacturers. These organizations face substandard medicine issues primarily because they fail to track purchased medicines. Emergency relief organizations deal with time-sensitive situations and, as a consequence, do not have time to efficiently track donations.

We identified seven international organizations as top financial players based on the information we found in the literature. The seven are the UN Children's Fund, the International Committee of the Red Cross, the WHO, Médecins Sans Frontières, the International Federation of Red Cross and Red Crescent Societies, the UN Development Programme, and the UN Population Fund. In addition to providing aid through medicine and medical supplies, these international organizations assist through technical expertise, training of local professionals, and medical research projects.

4.2.1. Organizations Providing Long-term Health Care

The most comprehensive regulation outlining guidelines for global medicine quality is the WHO's Prequalification of Medicines Program (PQP). Generally followed by international organizations, these guidelines are the only global medicines quality assurance program that ensure medicines purchased for humanitarian relief meet certain standards of quality, safety, and efficacy. The program maintains and annually updates a list of acceptable medicines and laboratories that meet standards around the world. To qualify for the list, a manufacturer must receive an invitation from PQP and submit a dossier with information regarding the quality, safety, and efficacy of its product. The information is then assessed by a team of WHO staff and experts. Before any decision is made, the manufacturing sites are inspected to verify that all WHO criteria are met. Only after a product passes all the tests is it placed on the WHO

list of prequalified medicinal products (World Health Organization 2010c). The main criticism of the WHO stems from Médecins Sans Frontières, which argues that the WHO focuses too heavily on counterfeit as opposed to substandard medicines (Médecins Sans Frontières n.d.).

The WHO strives constantly to improve PQP, mainly through procedural measures. In 2008, PQP updated the procedure for prequalification to increase transparency and accountability. The changes allowed for new tracks for the prequalification of zinc and influenza products. In 2010, PQP used survey results of manufacturers to develop a greater client focus. Some of these suggestions have already been incorporated, such as raising awareness of the opportunity for manufacturers to meet and consult with PQP assessors and clarifying procedures for resolving disagreements surrounding questions raised during the assessment of product dossiers (World Health Organization n.d.b). The WHO also initiated a study that highlights the benefits to manufacturers of registering products under PQP. To improve the quality of medicines, the WHO should constantly adjust and enhance PQP to meet new demands.

Three subsidiary bodies of the United Nations work to prevent and treat life-threatening diseases in developing countries. The Development Programme is the United Nations' global development network, working to increase knowledge, expertise, and resources for developing countries (UN Development Programme n.d.a). The Population Fund is an international development agency that promotes the right of every woman, man, and child to enjoy a life of health and equal opportunity (UN Population Fund n.d.). The Children's Fund works to provide quality education, protection against violence, and HIV/AIDS treatment for all children (UN Children's Fund n.d.). These three organizations are among the major UN programs that provide medicine to developing countries.

Although these three subsidiary bodies follow UN guidelines and transparency policies, they mostly serve as funding organs and do not always track how funds are expended. These organizations, particularly the Development Programme, emphasize transparency, demonstrated by their willingness to participate in aid effectiveness surveys (United Nations Development Programme n.d.b). Although prioritizing transparency helps with substandard medicine issues, the UN funds numerous programs, making it difficult to keep track of medicine purchases and destinations. To improve transparency, the UN should develop policies that trace funds to determine where and how they are spent in locally. This procedure would be costly at first but would ultimately help address the issue of substandard medicines. Additionally, the governing bodies of these programs should seek to increase their contact with local populations in order to ensure quality control procedures all the way to the consumer level.

4.2.2. Disaster and Refugee Relief Organizations

The International Red Cross and Red Crescent Movement comprises three main organizations: the International Committee of the Red Cross, International

Federation of Red Cross and Red Crescent Societies, and 187 or so individual national Red Cross Societies (International Committee of the Red Cross 2010). The main goal of the movement is to provide people in conflict areas with basic preventative and curative health care. Conflict not only results in casualties, but also in infrastructure damage, disruption in medicine supply, and increased numbers of refugees seeking safety (International Federation of the Red Cross and Red Crescent Societies n.d.). The movement also provides what can be described as a forum during which partners meet regularly to discuss common issues and share best practices. The International Red Cross and Red Crescent Movement also communicates with representatives of the states party to the Geneva Conventions at the International Conference of the Red Cross and Red Crescent. The agency should continue to communicate with other organizations to share ideas and improve procedures and delivery of medicine to those most in need.

Médecins Sans Frontières is committed to expanding access to lifesaving medicines, diagnostic tests, and vaccines, not only for patients in its programs, but also people assisted by other international programs. Médecins Sans Frontières accomplishes these goals through its Access Campaign, launched in 1999 (Médecins Sans Frontières 2012). Regarding substandard medicines, the organization is dedicated to explaining and clarifying the differences among substandard, counterfeit, and generic drugs. On Médecins Sans Frontières's website, Ellen 't Hoen, former policy advocacy director of the organization's Campaign for Access to Essential Medicines, explains the repercussions of confusing these categories of drugs (Médecins Sans Frontières n.d.). The media often discuss them as one problem with one common solution, but failing to propose different solutions tailored to each problem can have negative effects on policy formulation and consumer access to medicines.

4.3. National Governments

In this section, we analyze the effectiveness of regulatory regimes across developing countries and more closely examine the regulatory regimes of six countries—China, India, Thailand, Nigeria, Ghana, and Kenya. These six countries confront a significant presence of substandard medicines in their national markets. Evaluating the sources of and responses to substandard medicines in these countries informs our general analysis of the problem. As systematic global data on the prevalence of substandard medicines do not exist, we relied on our literature review of substandard medicines to make our country selection.

We did not look purely at estimates of prevalence of substandard medicines in making our selection. Instead we wanted to examine a balance of primarily exporters (India, China, and Thailand) with primarily importers (Nigeria, Ghana, and Kenya). We also wanted to look at countries whose characteristics vary in terms of medicines regulations, reforms, challenges, and successes. We preferred to have some geographic variety. Because a significant amount of the literature focuses on Asian and African countries, we chose these six.

Due to its size, China is a unique player in the pharmaceuticals market. In 2007, the Chinese pharmaceutical export trade was worth almost $25 billion. China exports finished medicines and raw materials used to manufacture active and inactive ingredients in medicines (Bate and Porter 2009, 1-2). Although estimates of the presence of substandard medicines in China vary greatly, even conservative estimates suggest large quantities of substandard medicines. We were also interested in knowing whether China's distinct political system affected its regulatory structure.

India is also a global supplier of medicines, with pharmaceutical exports totaling $10.3 billion in 2010 (Nair 2012). Like China, India has a reputation for counterfeit and substandard medicines. Our data show that India, along with China, is a primary exporter to African countries and a major source of substandard medicines there.

Thailand is a smaller exporter of medicines; the U.S. Pharmacopeial Convention in the Promoting the Quality of Medicines database identified Thailand as a key producer of substandard medicines.

Like China and India, Nigeria has gained notoriety for ineffective regulation of medicines. It is one of the largest economies in sub-Saharan Africa. The regulatory drug authority has undergone a series of reforms and has worked to clean up Nigeria's image as a regulator of medicines. (Innovations for Successful Societies 2009, 2-5). We were interested in how successful those reforms were and what current challenges are.

Ghana has a relatively complete set of laws, regulations, and guidelines, but has extremely high failure rates in quality control tests. We wanted to look into this. Similarly, Kenya generally shows high rates of substandard medicines in quality control tests. In 2008, during its sharing and expansion of the federal government between two major political parties, Kenya split its Ministry of Health (Luoma et al. 2010, 5). This politically motivated division of a major ministry is a unique regulatory environment that we decided to study further.

4.3.1. China

China is the world's largest producer of substandard and counterfeit medicines (Bate 2012a; Torstensson and Pugatch 2010, 10). Drug production is big business in the country, and the pharmaceutical industry is expanding rapidly. Between 1997 and 2007, value of the industry increased from $22 billion to $106 billion (Torstensson and Pugatch 2010, 22). The United States alone purchases more than $1.5 billion worth of drugs from China every year (Bate 2012a), and China produces not just the medicines themselves, but also the chemicals required for pharmaceutical production. In fact, 80 percent of the active ingredients for drugs sold in the United States are made in China (Hormats 2011).

Given the scope of the medicine manufacturing industry in China, it is particularly worrying that the country remains the largest producer of

substandards. Chinese manufacturers have perfected the art of producing substandards, even manipulating the composition of medicines to fool drug tests. In 2007 and 2008, for example, 95 people in the United States died of allergic reactions to contaminated heparin, a blood thinner produced in China. A toxic chemical had been added to the heparin to fool quality tests (Bate 2009).

Recently, China has been cracking down on substandard and counterfeit medicines. It has strengthened the State Food and Drug Administration, the country's primary medicine-related regulatory and enforcement agency responsible for registering new drugs and formulating policies regarding medicine production, composition and dispensation (Torstensson and Pugatch 2010, 23). The agency has been given additional resources to supervise and implement its regulations and to initiate investigations into and enforce penalties for violations (State Food and Drug Administration of China n.d.) Recent reforms have emphasized transparency, strict regulatory standards, and enforcement mechanisms. China also requires manufacturers to follow the WHO's Good Manufacturing Practices for pharmaceutical products and requires regulators to furnish manufacturers with certificates that show their compliance (Torstensson and Pugatch 2010, 24-25).

The State Food and Drug Administration has instituted a vast pharmacovigilance network, collecting reports of adverse drug reactions. Since 2002, local stations have been set up to monitor adverse drug reactions. The stations receive about 400 complaints per million people (Torstensson and Pugatch 2010, 24). The government has also made efforts to prove it is serious about cracking down on substandards and counterfeits. In 2007, for example, it executed the former director of the State Food and Drug Administration after he was found guilty of taking bribes to approve fake medicines (MSNBC.com 2007).

China's government has also tried to increase the number of regulators of drug manufacture and licensure. The Center for Drug Evaluation plays a key role in reviewing imported, generic, and over-the-counter medicines. Agencies like the National Institute for Control of Pharmaceutical and Biological Products and similar provincial-level agencies are entrusted with repeating experiments submitted with drug licensure applications to ensure the information is accurate (Deng and Kaitin 2004, 31).

In addition, China has tried to deter the production and sale of substandard medicines, increasing the penalties associated with such activities. Under current regulations, the penalty for offenses that result in "serious harm to human health" is imprisonment for three to ten years and a fine on the earnings from the drug sales. If drugs lead to death or especially serious harm, the punishment is a minimum of ten years' imprisonment, plus a fine on sales earnings. If the offense involves counterfeit medicines, the death penalty may be imposed (Zeldin 2009).

Despite these efforts, China remains the world's largest producer of substandard and counterfeit medicines (Bate 2012a; Torstensson and Pugatch 2010, 10).

Regulation remains inconsistent and continues to be undercut by corruption. Although formulation of drug-related policies and registration of new drugs and manufacturers are handled at the national level, monitoring and enforcement is carried out at the provincial level. As a result, local leaders are vested with significant power and can undermine the system through corruption. The system also lacks accountability and oversight of key regulation and regulators (Torstensson and Pugatch 2010, 45). Moreover, local leaders do not seem to have adequate pay or career advancement incentives to enforce drug regulation standards.

Like India, China has two fundamental problems with the drug regulatory system. First, the country is too large for a single regulatory agency to control it effectively. Second, the decentralized nature of the monitoring system means wide variation in regulatory effectiveness. As a result, implementation of standards is inconsistent, enforcement is weak, and accountability is limited (Bate 2009). Moreover, a significant part of the problem in China relates to counterfeits, and regulations alone cannot deter counterfeits, as producers are neither licensed nor legitimate. The sheer magnitude of the problem limits China's ability to control the production of substandards and counterfeits.

In outlining recommendations for China, therefore, we consider that China has a strong regulatory structure in place; policymakers just need to make it work (Torstensson and Pugatch 2010, 5). One possible solution is for the central government to create incentives for effective regulation at the provincial and other levels where monitoring occurs (Bate 2009). As with economic outcomes like growth, China could tie effective regulation of medicine manufacturing to local officials' salary and career advancement opportunities. This solution would minimize the effects of having such a decentralized regulation system. Additionally, the government could strengthen the penalties for corruption to prevent individual leaders from undermining the system. Finally, the government could regulate chemical manufacturing as well as drug manufacturing. As noted above, China is one of the largest exporters of drug-related chemicals, and substandard chemicals mean substandard medicines.

4.3.2. India

With China, India is seen as the leading manufacturer of counterfeit and substandard medicines in Asia (Khan and Ghilzai 2007). India has a strong and growing pharmaceutical sector, and between 1996 and 2006, pharmaceutical sales increased by 9 percent (Torstensson and Pugatch 2010, 26). Although drug manufacturers are required to follow the WHO's Good Manufacturing Practices (GMP), India is both a propagator and a victim of substandard medicines. Although estimates vary, research shows that a significant proportion of medicines in India are substandard. This proportion varies substantially by region: one study found that 12 percent of medicines in Delhi were substandard, but only 5 percent in Chennai suffered the same fate. A study carried out by the Indian

Ministry of Health and Family Welfare in 2003 found that 8 to 10 percent of medicines nationwide were substandard (Bate et al. 2010).[3]

The regional variation in substandard medicine proliferation is hardly surprising, given the structure of India's medicine regulatory and enforcement mechanisms. In India, state and national-level institutions are given different powers to monitor and enforce medicine production. The central government issues drug manufacturing standards, and a national institution, the Central Drugs Standard Control Organization, regulates clinical research and drug testing and authorizes new drugs. However, state-level agencies license and monitor drug manufacturing establishments and drug testing laboratories, regulate medicine quality, and approve drug formulations for manufacture (Central Drugs Standard Control Organization of India n.d.a). So, while GMP-based regulatory frameworks are set at the national level, enforcement and monitoring falls on state governments. As a result, there is significant variation in the effectiveness of state-level institutions, and one study found that 17 of 31 Indian states have functional drug testing laboratories (Khan and Ghilzai 2007). Of those 17 states, seven had laboratories that were reasonably equipped and staffed (Indian Ministry of Health and Family Welfare 2003).

Medicine quality also differs based on retail agency. One study in Rajasthan, a western state, found 6 percent of medicine samples collected from public distributors were substandard, but 14 percent of those collected from private retailers were substandard. In comparison, none of the samples collected from non-governmental organizations were substandard (Torstensson and Pugatch 2010, 16).

In principle, the Indian government has accepted multiple suggestions for reform. In 1975, for example, it accepted the recommendations of the Hathi Committee Report, which proposed the creation of a national drug authority that would be responsible for monitoring and regulating medicine manufacturing. This suggestion was subsequently repeated in the 1986 Drug Policy and the 1994 Drug Policy, but has yet to be implemented (Indian Ministry of Health and Family Welfare 2003).

Another aspect of the problem is that the risks of manufacturing substandard medicines are quite low in India. Under the Drugs and Cosmetics (Amendment) Act of 2008, penalties for producing counterfeits (called "spurious drugs" in India) were increased, but for substandards "criminal intent or gross negligence" must be proved before "administrative measures" or prosecution occur (Central Drugs Standard Control Organization of India n.d.b, 4). The general lack of regulation and enforcement combined with the extraordinary burden of proof

[3] A 2009 study commissioned by the same organization put the percentage closer to 1 percent (Central Drugs Standard Control Organization of India 2009). We consider this lower figure highly suspect, however, because the organization was not forthcoming with its methodology. Scholars like Bate believe the 1 percent figure is inaccurate (Bate 2010a; Bate 2010b).

required to show “criminal intent or gross negligence” means manufacturers of substandards are rarely caught, and even when they are caught, punishment is rarely meted out. As a result of inefficiencies in the Indian judicial system, cases remain undecided for years and rarely result in harsh punishment (Indian Ministry of Health and Family Welfare 2003, 4).

India does not use the same definitions as the WHO in distinguishing between substandards and counterfeits. Rather, it identifies “spurious medicines,” which include fake and adulterated medicines, and “grossly substandard” medicines, defined by percentage of active ingredient present (Central Drugs Standard Control Organization of India n.d.b, 2). Unlike the WHO definitions, therefore, these categories do not distinguish based purely on type of manufacturer, since legitimate manufacturers may produce adulterated drugs. As discussed, counterfeit and substandard medicines reflect very different weaknesses in regulation, weaknesses that can be addressed based on manufacturer. By blurring the line between legitimate and illegitimate manufacturers, India is trying to fight two problems with a single solution, which may explain why efforts to reduce the proliferation of substandard medicines have been largely ineffective.

Reforms implemented to reduce the proliferation of low quality medicines are geared more toward counterfeit than substandard medicines. For example, in 2011, the government passed legislation requiring medicine manufacturers to put 2-D barcodes on all packages to facilitate tracking and verification of authenticity of medication (Kannan 2011). These efforts may prove effective against counterfeiting but will be less effective against substandards as they cannot indicate the point in the supply chain where medicines began to lose effectiveness. Similarly, the government instituted a whistleblower scheme to reward individuals who report manufacturers of spurious medicines (Central Drugs Standard Control Organization of India n.d.c). Again, while the scheme may help reduce counterfeiting, it is unlikely to affect substandards because pinning culpability on legitimate manufacturers is harder.

The problem of substandard medication reaches well beyond India’s borders. Nearly half of a random sample of medicines tested in Nigeria, for example, did not meet British Pharmacopoeia limits for drug assay. Almost 40 percent of these medicines were manufactured in India. In 2003, when Nigeria threatened to boycott Indian medicines, India pledged to work specifically with Nigeria and increased vigilance of drugs for export (Raufu 2003). This example demonstrates the importance of aligning incentives: when the Indian government was given a strong economic incentive to improve performance, it did so.

As in China, the medicine regulatory system in India suffers from two fundamental problems: geographic size and decentralized regulatory structures. India lacks centralized enforcement of regulatory standards, and significant regional variation exists in the proliferation of substandard medicines. Distributors also vary significantly by type: public, private, or non-governmental

organization. Underlying these issues is the larger problem of a weak and non-comprehensive regulatory system and lack of adequate testing facilities. Although multiple reports have suggested the creation of a strong, centralized drug regulation agency, the government has yet to adopt such proposals.

Unlike China, India does not have a strong regulatory system in place. The division of labor between state and central government mandates gives states too much leeway in licensing, regulating, and enforcing medicine production. We recommend that the Indian government centralize drug and manufacturing licensing, while leaving states in charge of monitoring and enforcing regulations. The creation of a national drug authority has been suggested (and in principle, approved) twice, but has yet to be implemented (Indian Ministry of Health and Family Welfare 2003, 6). The new authority should adopt the WHO's definitions of substandard and counterfeit medicines.

Additionally we recommend that, as in China, state-level leaders in India be held accountable for drug regulation. However, unlike China, career advancement is not linked to economic and political outcomes, so India cannot depend on that system to control the problem. In India, accountability is to voters, so the government could engage non-governmental organizations and the media as partners in monitoring and spreading awareness of local leaders' effectiveness. Additionally, the government could increase the penalties for drug-related offenses (Indian Ministry of Health and Family Welfare 2003, 17). At the moment, such penalties are too weak, and manufacturers have no fear of getting caught. Lax penalties encourage corrupt practices; but harsher penalties could lead to better manufacturing practices. Finally, given India's role as a major exporter of medicines, administrative offices could be created to strengthen port offices, zonal offices, and testing laboratories (Indian Ministry of Health and Family Welfare 2003, 1).

4.3.3. Thailand

In response to problems with substandard medicines in Thailand, the 1987 revision of the 1967 Drug Act was passed to improve drug quality and eliminate substandard and counterfeit medicines (Thai Food and Drug Administration n.d.). The law covers the supply side of the drug supply chain: manufacturers, importers, and retailers. Manufacturers are required to obtain manufacturing, wholesaling, and advertising licenses, together with registration for each medicine they want to make, prior to the start of manufacturing . Medicine importers are required to obtain wholesaling and advertising licenses and registrations for imports. Retailers (including pharmacies) are required to obtain sales licenses to start their businesses (Thai Food and Drug Administration 2008, 26).

The results of the 1987 Drug Act were not as positive as expected. Substandard medicines remain an issue today. According to the Thai Food and Drug Administration (FDA) (2008, 28), 13 percent of medicines sold in 2003-2005 in Thailand were substandard. Two major weaknesses that lead to problems with

substandard medicines are outdated regulations and poorly functioning regulatory regimes.

An example of an outdated regulation in the Drug Act is the section on licensing of drug advertising. As the act does not regulate Internet advertisement licensing, non-licensees can freely advertise their medicines (which could be substandard) on the Internet. According to the Thai Drug Watch (2011, 90), more than 85 percent of medicine advertisements on the Internet are run without permission from the Thai FDA. This unregulated online medicine advertising increases the chance of ill-informed consumption of substandard medicine in Thailand.

Thailand's poorly functioning regulatory regimes can be analyzed at two levels: individual and system. At the individual level, we cannot find strong evidence pointing to particular agencies that are inefficient or not well functioning, but storage and transportation facilities appear to be part of the problem. One finding estimates 5 percent of all drugs prescribed in Thailand are substandard due to improper storage, mishandling, and other logistical problems. One pharmacist reveals that problems with substandard medicine in Thailand shifted from the manufacturing process to transportation and storage since the Thai government started implementing several policies to improve manufacturing, such as the national drug list and Good Manufacturing Practice. Another pharmacist suggests that transparency and monitoring are keys to solve the problem of poor regulation (Sukin 2007).

At the system level, Sukin's research implies that the key players in the drug supply chain responsible for this problem are manufacturers (because they take care of storage after manufacturing and before transportation) and terminal suppliers (which include hospitals and pharmacies). Sukin's results suggest that related agencies need to work more efficiently on monitoring these key players. As most of these agencies are under an umbrella of the Thai FDA, it is the Thai FDA's responsibility to supervise them closely. At the system level, as mentioned in the Thai FDA report (2008, 28), the problem lies with agencies not cooperating to prevent and suppress substandard medicines.

Poorly functioning regulatory regimes are not only a domestic problem but also an international problem, especially for neighboring countries. According to the results of the Medicines Quality Database (shown in Table B1), five of seven substandard antimalarial medicine manufacturers whose products were sampled in Cambodia are located in Thailand. With 85 percent of its sampled antimalarial medicines proven substandard, Brainy Pharmaceutical Limited Partnership seems to be the dominant player in Cambodia's drug market. Supporting results from the database, Lon and others (2006) reveal that 77 percent of failed quinine (one type of antimalarial medicine) samples are labeled as products of Brainy Pharmaceutical. Cambodia's substandard medicine situation would be less dire if the regulatory agencies in Thailand were better at monitoring unregistered substandard medicines. However, the Thai FDA has responded to this problem by

confirming officially that Brainy Pharmaceutical is not a legitimate manufacturer in Thailand (Lon et al. 2006). The same response also appears on the Thai FDA website. The manufacturer's name and address are false (Thai Bureau of Drug Control 2004). Although the location of Brainy Pharmaceutical cannot be proven, the fact that its labels are written in Thai suggests Thai origin. Thailand needs to target an improvement in efficiency of regulatory regimes.

To combat substandard medicines, the Thai FDA has implemented several projects in the past five years. As manufacturing processes used to be the major cause of substandard medicine problems in the country, some projects, such as promoting Good Manufacturing Practice, were created to continue improving medicines quality during manufacturing. As a part of the license approval process, manufacturers need certificates to prove that their processes are closely controlled and follow Good Manufacturing Practice (Thai Food and Drug Administration 1999, 14). Some projects, such as the medicine quality assurance project, are designed to assure the quality of medicines for domestic consumption by targeting the whole supply chain. These projects work on quality assurance of drug manufacturing, public communication on drug quality, and drug monitoring systems (Thai Food and Drug Administration 2008, 28).

Problems with substandard medicines mainly occur during transportation and storage; they also occur during manufacturing. To strengthen quality control, Thai Drug Watch (2011) and Sukin (2007) propose four solutions: the revision of drug formula registration; the Single Window project; Good Pharmacy Practice; and greater public awareness of drug quality control and monitoring.

One objective of revising drug formula registration is to mitigate the problem of instability and insolubility of medicines' active ingredients. Having the standard of each medicine's solubility written on the drug formula can inform manufacturers of the level of solubility of active ingredients their medicines should have to qualify for sale (Thai Drug Watch 2011, 27).

The Single Window project is Thailand's new drug watch system. It replaced a paper-based system with information technology tools to help health-related agencies communicate and exchange drug quality information. Hospitals, the Thai FDA, and provincial public health offices can share the most up-to-date information on medicines' quality. When any substandard medicines are found, monitoring agencies and hospitals can be warned immediately, be advised on how to treat those substandard medicines, and be able to access the drug quality database at the same time. This project is believed to support the monitoring system of the whole supply chain (Thai Drug Watch 2011, 42-43).

The third solution is promoting Good Pharmacy Practice, which outlines minimum standards for pharmacists. The Thai Drug Watch (2011, 78) suggests that the Thai FDA accelerate the enforcement of ministerial regulations on Good Pharmacy Practice. As stated in the International Pharmaceutical Federation

website, the primary role of pharmacists, which should be included in the Good Pharmacy Practice standard, is preparing, obtaining, storing, securing, distributing, administering, dispensing, and disposing of medical products. By enforcing Good Pharmacy Practice, the Thai FDA could control the quality of drugs during storage in the pharmacy more effectively.

Another solution is promoting public awareness of drug quality control and monitoring. Sukin (2007) suggests that the government can use the Internet to educate the public by publishing information on drug quality. Also, the government can list on a website drugs whose quality is approved instead of posting a list of substandard drugs (Sukin 2007).

4.3.4. Nigeria

Nigeria has the regulatory framework in place to comprehensively regulate the import, export, manufacture, advertisement, distribution, sale, and use of regulated medicines. The national medicines regulatory agency, the National Agency for Food and Drug Administration and Control (NAFDAC), is mandated to formulate regulations and guidelines; register products; test products to determine identity and quality; exact fines (Nigeria National Agency for Food and Drug Administration and Control n.d.); license manufacturers, wholesalers, and distributors (Nigeria Federal Ministry of Health 2011, 25); and inspect products and local manufacturing premises, wholesalers, retail distributors, and pharmacies and dispensing points that are attached to medical facilities (Nigeria Federal Ministry of Health 2011, 15). The agency's goal is "to eradicate fake drugs and other substandard regulated products" (Nigeria National Agency for Food and Drug Administration and Control n.d.). With 1,500 permanent staff members as of 2010 (Nigeria Federal Ministry of Health 2011, 14), NAFDAC occupies a central office, six zonal (regional), and 36 state offices.

Nigerian pharmaceutical regulations are so poorly implemented that the country has become famous as a hotbed of counterfeit and substandard medicines. Sixty to seventy percent of drugs sold in Nigeria in 2001 were estimated to be fake, substandard, adulterated, or expired. Countries across Africa banned Nigerian imports (Adinuba 2003; Innovations for Successful Societies 2009, 4). When Dr. Dora Akunyili was appointed director general of NAFDAC in 2001, she embarked on reforms. She restructured NAFDAC and dismissed officials known to be corrupt (Innovations for Successful Societies 2009, 2-5). Akunyili re-trained staff, opened state offices to improve accessibility, and refurbished drug analysis laboratories to make them more functional. NAFDAC began to enforce drug regulations more strictly, garnering support from the public (Garuba et al. 2009, 2).

The agency further improved its image by making a series of very public and valuable seizures and destruction of counterfeit and substandard medicines. NAFDAC produced guidelines for companies and individuals to know the procedures for applying for licenses and registrations, and it organized public awareness campaigns, including one that directed citizens to check expiration

dates and to authenticate the NAFDAC certification number before taking any medicine. The importance of these reforms is partly illustrated by the fact that multiple attempts were made on the lives of Akunyili and her immediate family, and several NAFDAC offices were burned in the early 2000s (Innovations for Successful Societies 2009, 2-6).

The accompanying reduction in counterfeit and substandard drugs (the extent of which is debated) allowed for growth in the domestic manufacturing sector (Innovations for Successful Societies 2009, 4). However, as of 2009, domestic manufacturers produced less than one third of the drug supply, with the bulk of the remainder being imported from India and China (Garuba et al. 2009, 2). Additionally, Nigeria does not produce the raw materials used in medicines manufacture, so it imports these as well (Echenim 2011). As a result, the Ports Inspection Directorate is vital in protecting Nigerian markets from substandard medicines.

It is alarming, then, that the NAFDAC Ports Inspection Directorate is not allowed access to the ports. In June 2011, the Nigerian Ports Authority introduced joint inspections to reduce processing time. Some security and regulatory agencies, including NAFDAC, objected to the joint inspections and refused to participate (Airahuobhor 2011). NAFDAC and several other agencies were subsequently banned from operating in the ports. Although NAFDAC struggles with corruption and poor implementation of regulations, without a direct presence at the port, the agency is left powerless to regulate imports at all.

Online news articles and opinion columns accuse NAFDAC officials at all levels of a variety of corrupt practices. In a 2009 survey, stakeholders and officials in the pharmaceutical sector, including NAFDAC, report that bribery and favoritism are “common” at ports during product registration, and that “it is not uncommon for [manufacturing site] inspectors to be impersonated.” Manufacturing site inspectors often receive gifts and transport from companies being inspected. The offer of transport is a possible sign of corruption, but it also represents a safety hazard for officials (Garuba et al. 2009, 8).

Threats and acts of violence are inflicted on NAFDAC officials at ports and many other phases of the regulatory process (Garuba et al. 2009, 5-8; Nigerian Food and Drug Regulatory Advisor 2010b). Corruption survey respondents also reported that many pharmacies are run by businesspeople who hire pharmacists as a front to “intimidate their way through normal regulatory procedures” and sell substandard medicines at a large profit. Although some offenders are prosecuted, the business is lucrative and most are not discouraged (Garuba et al. 2009, 9).

Corruption and intimidation are two factors contributing to low compliance and enforcement of regulatory policy, which is deemed “inadequate” by the Health Ministry itself (Nigeria Federal Ministry of Health 2010, 3). The law requires some transparency: NAFDAC is required to post and update public lists of registered medicines. The law does not require similar disclosure of licensed

pharmaceutical facilities or certified warehouses, wholesalers, and distributors (Nigeria Federal Ministry of Health 2011, 14-25).

The agency could achieve greater transparency of operations in a few ways. The agency could require officials to disclose conflicts of interest in any of its operations, and it could publish best practice guidelines for each actor in the supply chain, not just for manufacturing licensure. (Nigeria Federal Ministry of Health 2011, 10-25). NAFDAC also does not disclose the results of external or internal audits (if indeed they occur at all) or qualifications requirements for its staff positions. The agency could require publication of each and introduce sanctions for non-compliance (Garuba et al. 2009, 1-8).

Nigeria's medicines supply system would be difficult to regulate under any circumstance. Public sector procurement takes place centrally for therapeutic classes related to HIV, malaria, and tuberculosis, while individual health-care institutions procure and store other medicines (Nigeria Federal Ministry of Health 2011, 25). Final distribution occurs at thousands of distributors, pharmacies, "shops" (which are not supervised by a pharmacist), and ambulatory venders (World Health Organization 2010a, 22). NAFDAC does not have the capability to regulate the variety of distributors in the market. Retail distribution of drugs "has been described as chaotic and is virtually unregulated" (Garuba et al. 2009, 9).

In addition to the difficulty of regulating many players, NAFDAC confronts systemic and logistical factors that may degrade medicines. Following sea transit, the medicines are slowly processed at ports, and land transport is slowed by fuel shortages. Many warehouses are not equipped to handle medicines sensitive to temperature and humidity, and retailers are even less well-equipped. Rural retailers in particular may not have electricity or telecommunications (Garuba et al. 2009, 9).

The primary cause of low compliance with regulatory policy is lack of enforcement. This stems from NAFDAC's lack of personnel and training to manage a decentralized supply chain, as well as continuing problems with corruption fed by lack of transparency and intimidation of officials. NAFDAC's limited efforts to improve transparency at all levels and its quarrel with the Nigerian Ports Authority may signal a lack of will to regulate effectively. To preserve its newfound status as a reformer, NAFDAC could agree to perform joint inspections in ports to reach an agreement with the Ports Authority and regain access to ports. NAFDAC could improve transparency by publishing results of external and internal audits and qualifications requirements for staff positions. It could also create, make public, and enforce conflict of interest guidelines. These steps would serve to increase the public trust and to ensure that NAFDAC undertakes audits and hires the most qualified personnel. NAFDAC could continue to invest in improving staff training, as it has since 2001 (Garuba et al. 2009, 1-10). Although comprehensive laws and regulations are in place, producing best practices guidelines would provide a detailed framework of

compliance for both officials and pharmaceutical actors (Nigeria Federal Ministry of Health 2011, 10-25).

4.3.5. Ghana

The major regulatory agency for medicines in Ghana is the Food and Drugs Board (FDB). The Food and Drugs Act established the board in 1992, but it was only inaugurated in 1997 (Ghana Food and Drugs Board n.d.a). The FDB is mandated to register, approve, and monitor medicines (Ghana Food and Drugs Board n.d.f). As Ghanaian pharmaceutical exports were a mere 0.3 percent of Ghanaian imports in 2011 (NOSIS Research and Development Laboratory n.d.), we consider that the problem of substandard medicines is not exported. While this figure captures formal market trade only, during the course of research we found no evidence of illegal exports from Ghana.

The FDB shows a number of strengths. It provides a thorough set of guidelines on its website, instructing on registration, licensure, storage, safety and quality testing, importation, exportation, and related topics (Ghana Food and Drugs Board n.d.c). The board publishes lists of registered drugs (Ghana Food and Drugs Board 2011). The regulatory framework requires transparency and accountability, and the FDB has a code of conduct. Quality management guidelines require testing of medicines at registration, importation, and in post-market surveillance (Ghana Food and Drugs Board n.d.c).

The board lacks the capacity to enforce many regulations and guidelines (Ghana Ministry of Health 2004). For example, although it runs a central laboratory and quality control outlets, in 2006 the labs received a mere 19 samples for testing (National Drugs Programme 2009, 54). The standard test for quality is, in fact, to verify product registration with the FDB or to verify that products are procured from pre-selected suppliers, rather than running laboratory tests on quality (Ghana Ministry of Health 2011). The FDB should develop procedures for regular submission of samples to laboratories capable of running quality testing, which may be limited to the central laboratory. The FDB needs sufficient resources to staff and equip laboratories adequately and to provide transport of samples if necessary.

A 2011 WHO survey of antimalarial medicines quality found that Ghana, with a 40 percent failure rate overall, shows a higher failure rate for registered medicines (52 percent) than unregistered (20 percent). We speculate that the prominence of registered substandard medicines indicates either corrupt favoritism in the registration process or a prevalence of counterfeit medicines labeled as registered Ghanaian medicines. The WHO also found that roughly half of imported medicines, which are predominantly of Indian and Chinese origin, and one-quarter of domestic medicines are not registered (World Health Organization 2011, 8 and 54). Although registered medicines show a higher incidence of substandard quality than unregistered, substandard rates for both registered and unregistered medicines are high and represent a very serious problem. The survey

results show a great need for increased monitoring both at ports and at facilities of domestic actors throughout the supply chain. To so dramatically increase the monitoring and inspection role of the FDB, the agency requires additional qualified personnel and financial resources to train personnel adequately, pay their salaries, transport them to inspection sites, and process paperwork for increasing numbers of inspections and (presumably) violations.

The WHO survey found the highest percentage of failures (59 percent) in the southern zone, which is nearest to ports and populated most heavily. This zone would theoretically be home to the most highly qualified practitioners and officials. These results suggest that medicinal deterioration occurring in transit and at warehouses and retail outlets in areas of poor infrastructure is not a significant problem in Ghana (World Health Organization 2011, 25), although Arhinful (2009) found in a nationwide survey of health-care facilities that 33 percent of private drug outlets and 20 percent of public distributers used low-quality storage conditions. Arhinful found no expired medicines. WHO testing in 2011 showed no significant improvement over results from testing in 2003 (World Health Organization 2011, 57).

Improving quality assurance in Ghana is made more difficult by the high number of retailers. In its revised 2004 National Drug Policy, the Ministry of Health highlights the "dramatic increase in the number of drug outlets in both the public and private sectors" (Ghana Ministry of Health 2004, 1-2). Approximately 11,000 licensed private pharmacies and medicines outlets distribute medicines to patients from public, private, and mission health facilities (Arhinful 2009, 12-13; World Health Organization 2010a, 23). The Ministry of Health describes challenges to effective regulation as permeating the system. It identifies a weak and under-resourced regulatory regime with low enforcement capabilities, poor compliance, lack of qualified management and technical staff, lack of continual training and learning opportunities for staff, unarticulated drug supply management procedures, and lack of quality distribution and storage facilities (Ghana Ministry of Health 2004, 1-2).

The ministry responded by establishing the National Drugs Programme, the National Drug Policy, the National Essential Drugs List, and Standard Treatment Guidelines. The ministry also hired regional experts to teach appropriate drug use and train pharmacists (Ghana Ministry of Health 2004, 1-2). Although the FDB has advanced in prescribing guidelines and procedures for various regulatory processes, as well as in providing higher quality distribution and storage facilities, several senior officials at the Ministry of Health report that as of 2007 there was a lack of political will to implement most components of the National Drug Policy (Harper and Gyansa-Lutterodt 2007, 26).

Following the 2011 WHO antimalarial assessment, national stakeholders (including FDB officials) committed to raising public awareness about medicines quality issues and supported the FDB to regulate more effectively, invest in

human resource development, and require quality certification of raw materials imported for local manufacturing. The FDB agreed to share its database of registered medicines with other stakeholders so that facilities and prescribers could avoid unregistered medicines (World Health Organization 2011, 60). This commitment may be the reason for inclusion of a registered medicines list on the FDB website; if so, it should be updated more regularly to be effective. As of May 2012, the list displayed dates from March 2011. The follow-through and effectiveness of other commitments has not yet been reported on.

Although Ghana has codified the necessary legal framework and regulatory procedures, the lack of political will reported by officials at the Ministry of Health leads to a variety of interrelated problems and endangers the success of solutions.[4] This lack of will can also be described as misalignment of incentives to regulate properly: regulators do not receive sufficient incentives from consumers, national interest groups and authorities, or the international community. FDB officials poorly enforce medicines regulations because of financial and human resource deficiencies: personnel, equipment, and facilities are insufficient to carry out inspections and effective quality control tests; poor training and lack of will to monitor and correct FDB officials' behavior leads to poor job performance and conceivably to favoritism or other forms of corruption

Poorly enforced regulations allow unregistered and substandard registered medicines to pervade the market. To reduce these in the supply chain, the FDB must greatly increase inspections and effective quality testing at ports and facilities of domestic actors in the supply chain. Monitoring is made more difficult by the large number of retailers in Ghana. To effectively monitor, the FDB requires additional personnel and financial resources for personnel training, transport, and salaries, as well as for higher administrative costs of increased volume of inspections and violations. FDB officials would of course need to enforce consequences for violations. The same lack of political will that leads to poor enforcement also signifies that funding and institutional capacity for expansion of a professional workforce likely are lacking.

When faced with poor political will, policymakers can consider ways to enable consumers to be part of the regulatory process, create internal incentives to regulate, or create external incentives to regulate.[5] In Ghana's case, the national

[4] Lack of political will is a difficult and common problem in public health in many developing countries, as found in this study and in a 2004 report by the U.S. General Accounting Office (28). The Institute of Medicine finds that "product safety is not a high priority in countries with skeletal health systems, poor sanitation, and high mortality" (Riviere and Buckley 2012, 3). Increased foreign aid for health has only lead to recipient governments decreasing their allocations to the health sector.

[5]The sources consulted for this study did not offer recommendations directly responding to the problem of political will. Recommendations encouraged the Ghanaian government to hold public awareness campaigns on medical quality issues, increase investment in the material and technical aspects of regulation, improve implementation of regulations, and complete self-assessments of the regulatory system (WHO 2010a; WHO 2011).

stakeholders' meeting partly addressed two of these avenues: the public should become more informed with public awareness campaigns of medicine quality issues and the publication of the registered medicines database. The stakeholders' commitments to supporting the FDB to regulate more effectively and invest in human resource development, while admittedly vague, may provide internal incentives for improvement. Even if acting alone, committed leadership at the FDB should mobilize competent personnel to train, monitor, and respond strictly to infractions on the part of the FDB workforce. This small group would need sufficient compensation and full support of leadership. With improved knowledge and behavior, a more professional FDB workforce would be capable of enforcing regulations. If the FDB leadership lacks the will, members of the international community should create incentives for making the same improvements in human and material resources by (for example) committing to invest in Ghanaian medicine manufacturers following independently confirmed improvements in material resources for regulation, professional quality of FDB staff, enforcement trends, and prevalence of substandard medicines in the market.

4.3.6. Kenya

Kenya receives large amounts of donor aid for health initiatives and has high infection levels of HIV/AIDS, tuberculosis, and malaria. As a business climate, Kenya suffers from corruption, counterfeit products, and a high cost of doing business (Luoma et al. 2010, 1-4). Kenya has been the subject of several research studies, and there are many tested sample results of medicines procured within Kenya. (For a list of studies, see Appendix A.) Testing done on Kenyan medicines shows substandard medicines failure rates as high as 46 percent.

The main bodies of health policy in Kenya are the Ministry of Medical Services and the Ministry of Public Health and Sanitation. These two ministries resulted from the division of the Ministry of Health in 2008. According to the Kenya Health Services Assessment by the Health Systems 20/20 cooperative agreement with the U.S. Agency for International Development (USAID), this split in ministries was politically motivated and has caused duplication, confusion, and competition for funding and resources. With regard to pharmaceuticals and medicine, the Ministry of Medical Services is responsible for "regulatory bodies for pharmacy and medicine," and the Ministry of Public Health and Sanitation is responsible for "health inspection" and "government pharmacists" (Luoma et al. 2010, 5).

Kenya's government pharmaceutical policies date to 1957 with the passage of the Pharmacy and Poisons Act, which created the Pharmacy and Poisons Board. Independent of the two ministries, the board is responsible for regulation and enforcement. Established in 1994, the Kenyan national drugs policy has been poorly implemented, and it lacks many key management elements for it to be successful. Kenya is drafting a second national pharmaceutical policy (Luoma et al. 2010, 45-48).

The Kenyan government procures and distributes a large portion of pharmaceuticals through the Kenya Medical Supplies Agency. Funding for these purchases is provided by government financing, subsidized user fees, donor contributions, and private spending (Luoma et al. 2010, 19-20).

Kenya's pharmacovigilance team from the Pharmacy and Poisons Board began a media campaign in 2011 to encourage Kenyans to buy medicines only from registered pharmacies. Pharmacists and pharmacy technologists are identified in Kenya by government-issued green and blue badges and by a certificate that must be in plain sight at the pharmacy. However, the board admits that these procedures only alleviate part of the problem with substandard medicines, as they can still be found in registered pharmacies, and counterfeit government green and blue badges have been discovered. In the last two years, the board's simple reporting system for substandard and counterfeit medicines has received more than 190 reports, which has led to product recalls and arrests (Esipisu 2011).

Samples from the Medicines Quality Database show Kenya's problem with substandard medicine to be as recent as 2010. Kenya's two main problems that prevent the government from effectively combating substandard medicines are its disjointed health ministry structure and a lack of a comprehensive medicines policy. In the creation of new medicines legislation, Kenya needs to recognize substandard medicines as an issue and create steps to regulate and enforce medicines within its borders. The 1957 Pharmacy and Poisons Act and the 1994 National Drugs Policy need to be updated with proper implementation and enforcement mechanisms built in.

Table 1 identifies trends in the problems facing the six countries analyzed above and some of the potential policy responses that we identified in this section of the report. Many of the problems described here follow a causal chain. The first category below, "political," identifies the source problem, and other categories may include intermediate and end-of-chain problems. Our proposed policy responses to these intermediate and end problems may therefore appear not to address the source of the problem, particularly relating to political will. Proposed responses are not necessarily adequate to resolve the identified problem. Comprehensive recommendations, with more detailed analysis of causal chains, appear in Section 5 of this report.

Table D1 in Appendix D summarizes regulations and enforcement mechanisms for medicines in China, India, Thailand, Nigeria, Ghana, and Kenya. Table D2 summarizes regulatory weaknesses, efforts to combat substandard medicines, and our proposed policy responses for each country.

Table 1: Trends in Problems Related to Substandard Medicines and Possible Policy Responses

Common Weaknesses in Regulatory Regime		Authors' Proposed Policy Responses
Political	- Lack of political will to regulate effectively	- Involve public to increase transparency and educate public about substandard medicines quality - Engage non-governmental organizations and media to hold leaders accountable for establishing and enforcing regulatory standards - International community may create incentives for change through conditional investment or other mechanisms (discussed in recommendations)
Institutional	- Lack of enforcement of regulations	- Increased legislative attention to formulating medicines-related regulations - Increased resources devoted to regulatory and enforcement agencies
	- Corruption and/or lack of transparency	- Establish and enforce conflict-of-interest guidelines - Involve public to increase transparency: publish internal and external audits; publish professional requirements for agency positions
	- Lack of punishment of staff for infractions or corruption	- Increased penalties for corruption
	- Lack of punishment of staff for low-quality work	- Increased consequences for low-quality work
Legal/ Procedural	- Inadequate legal or regulatory framework	- Address gaps in laws and regulations - Produce good practice guidelines for supply actors
	- Outdated regulations (such as for registration, monitoring, and advertising)	- Update regulatory framework
	- Minimal penalties for producing substandard medicines	- Increased penalties and enforcement
Structural	- Conflicting responsibilities and/or poor coordination between related agencies or ministries	- Consolidate authority for regulations and licensure - Increase medicines information accessibility for related public agencies
	- Regional disparities in regulation and enforcement	- Establish career-related incentives for local leaders to regulate effectively
Resources	- Lack of material resources to inspect or run laboratory quality checks	- Increase staff and equipment for increased monitoring at all stages of supply chain - Establish administrative offices to strengthen port offices, zonal offices, and testing laboratories - Encourage or require procurement of medicines from proven manufacturers
	- Low human capital due to poor training of staff	- Increase staff and equipment for increased monitoring at all stages of supply chain - Improve staff training and material resources

Sources: Authors. Based on data from State Food and Drug Administration of China (n.d.), Torstensson and Pugatch (2010), Bate and Porter (2009), Central Drugs Standard Control Organization of India (2009, n.d.a, n.d.b, n.d.c), Partnership for Safe Medicines India (n.d.), Ghana Legal Environmental Information (n.d.), Ghana Food and Drugs Board (n.d.a, n.d.b, n.d.c, n.d.d, n.d.e, n.d.f), GhanaWeb (2011), Ghana Ministry of Health (2004, 2011), Global Health Consulting Group (2009), National Drugs Programme (2009), Ghana Business New (2012), Nigeria Federal Ministry of Health (2011), NAFDAC Nigeria (n.d.a., n.d.b, n.d.c., n.d.d., n.d.e., n.d.f.), Nigerian Food and Drug Regulatory Advisor (2010a, 2010c), Ugwoke (2012), World Health Organization (2011), Garuba et al. (2009), Luoma et al. (2010), Thai Food and Drug Administration (1999, 2008, n.d.), Thai Drug Watch (2011), and Sukin (2007).

5. Recommendations

Section 4 discussed case studies for three important actors (manufacturers, international organizations and national governments) involved with the manufacture, purchase, and regulation of substandard medicines. In that section, we outlined recommendations specific to each actor. In this section we present broader recommendations, to be implemented at the international level.

The problem of the spread of substandard medicines is hard to resolve because, although it has international ramifications, there are no international enforcement and/or regulatory agencies. Additionally, medicines may be rendered substandard at any point along the supply chain, which implicates a number of actors including international organizations, manufacturers, national governments, non-governmental organizations, transporters, warehouse facilities, retailers, etc. in both the problem and the solution.

At its very core, the problem of substandard medicines is a problem of misaligned incentives that lead to market failure and government failure. International organizations and consumers have an incentive to purchase and consume good quality medicines, but other actors along the supply chain have an incentive to cut costs. Since we cannot rely on international enforcement mechanisms, many of our recommendations outline ways in which actors can align incentives so others along the supply chain will diminish the spread of substandards. Better aligned incentives can help alleviate the problem of a lack of international enforcement mechanisms because it encourages actors to self-regulate.

We make three overall recommendations. First, we make specific suggestions on bringing national governments' and manufacturers' incentives in line with those of procurers and consumers. Second, we outline ways in which manufacturers, procurers, and distributors can better monitor medicine supply chains. Finally, we recommend that governments, international organizations, and researchers clarify the differences between substandards and counterfeits and increase their emphasis on substandards.

Many of our recommendations involve the WHO, a central player in coordinating the health-related activities of international organizations, national governments, and non-governmental organizations, and in carrying out pharmaceutical research. Additionally, with 194 member countries, the WHO is arguably the best platform for discussing and implementing international-level policies and recommendations.

Below we detail our recommendations in order of importance. They are to align incentives across the medical supply chain, to improve overall supply chain management, and to clarify the definition of substandard medicines and increase emphasis on fighting them.

1. **Align incentives across the medical supply chain**
   Actors along the supply chain have differing incentives with respect to medicine quality. Here, we address ways in which to bring manufacturers' and national governments' incentives in line with those of procurers and consumers.

   - **Create incentives for national governments to tighten regulatory and enforcement mechanisms:** As our country case-studies show, some of the worst exporters and importers of substandard medicines have regulatory frameworks in place, but they do not function well enough. Two issues lie at the core of the problem of poor enforcement. First, developing countries may not have the resources to run comprehensive regulatory systems. Second, they may not have the incentives to do so. Both issues have to be addressed to stop the spread of substandard medicines.

     To increase resources for regulation:

     - Certain types of developmental aid should be set aside for governments committed to improving their regulatory and legal institutions, including adopting and enforcing Good Manufacturing Practices and Good Pharmacy Practices guidelines. This aid should be tied to measurable outcomes regarding the strength of medical regulatory and legal regimes, which will vary based on a country's circumstances.
     - Special funding should be set aside for countries that propose concrete plans for implementing national projects that give consumers a chance to participate in the identification of substandards and counterfeits.

     To create incentives for nations to tackle substandard medicines, the WHO should publicize poor manufacturing and regulatory performance by manufacturers and governments. Medicine procurers could then patronize countries and manufacturers with the cleanest manufacturing records (i.e., those that produce the fewest substandard medicines). This business would create incentives for manufacturers and governments to improve regulatory and enforcement structures. To create incentives:

     - The WHO should carry out systematic, regular, and ongoing research about which developing countries and manufacturers produce the best quality medicines for the lowest price. This research should include regular quality testing.
     - In addition to identifying high quality manufacturers, the research should lead to the production of a list of poor quality manufacturers, made publicly available.

- This research should be ongoing, so that if blacklisted countries or manufacturers improve the quality of their medicines, procurers can take such changes into account.
- International agencies and public procurement sectors of developed countries could coordinate purchases and use their monopsony power to pressure low-performing countries or manufacturers.

Such ongoing research would create an external check on countries' and manufacturers' regulatory performance and create economic incentives for effective regulatory regimes.

❖ **Create incentives for manufacturers to self-regulate:** To encourage medicine manufacturers to uphold high production standards, procurers should patronize manufacturers based on their ability to consistently produce high quality medicines. Fund-granting agencies and large pharmaceutical buyers should require procurers to research which manufacturers have the best production records. To determine which manufacturers to buy from, procurers should:

- Use existing tools, like the WHO's Pre-Qualified Medicines list and the U.S. Pharmacopeial Convention's Medicines Quality Database. This database could also be made more user-friendly to allow potential procurers to perform quick searches into manufacturers.
- Consult the ongoing medicines quality research.
- Patronize manufacturers based on transparency, supporting those who are clear and open about their manufacturing and monitoring practices.

We understand that political factors limit procurers' ability to use these tools. These factors include trade and other kinds of treaties, sources of funding and accompanying stipulations, and efforts to support local producers. Although we do not expect procurers to ignore political realities, we recommend they use tools as much as possible to determine the range of options available to them to ensure they buy and distribute high-quality medicines. By doing so, they will create incentives for manufacturers to self-regulate.

Finally, to create economic incentives for manufacturers in developing countries to improve their practices, procurers could:

- Approach manufacturers in developed countries to see if they can match prices for medicines made in developing countries.

These companies may be willing to match prices if the distribution of low-priced medicines is tightly controlled so as not to create black markets in the developed world. Involving manufacturers in the developed world is crucial, because they consistently produce

better quality medicines. If these companies are willing and able to match the prices procurers pay for medicines from the developing world, manufacturers in the developing world will have to improve production standards or lose customers.

2. **Improve overall supply chain management**
   Instead of operating independently of one another, actors along the supply chain should be given incentives to monitor each other, especially manufacturers and procurers, who often do not take responsibility for medicines once they leave their possession. Distributors must also be monitored; non-state actors could play a key role in such oversight.

   - **Manufacturers:** As the first stop along the supply chain, manufacturers have a dual responsibility. First, they must ensure ingredients are of good quality; second, they must ensure medicines maintain their quality along the supply chain. Pharmaceutical products are only as good as their ingredients. Manufacturers should:
     - Carefully monitor and routinely test the quality of the ingredients they buy.
     - Monitor medicines after they leave the point of production by working with well-established and trustworthy transporters, warehousing facilities, and retailers.
     - Carry out routine and surprise tests at various points along the supply chain to ensure the integrity of medicines quality.
     - Communicate all along the supply chain the information necessary for medicines to work effectively (correct dosage and labeling).

     To improve consumer and procurer confidence every manufacturer, like Novartis, should be transparent about its medicines monitoring procedures and policies. Manufacturers could:
     - Prominently display information on how they monitor pharmaceutical inputs and outputs on their websites.
     - Enable consumers to report on company websites where they bought medicines they suspect to be substandard or counterfeit.

   - **Procurers:** As discussed in sections 3 and 4, international actors often procure medicines but rely on local actors for distribution. Procurers need stronger follow-up procedures to monitor what happens to medicines once they have been handed over to local distributors. Medicines should be followed from the point of manufacture to delivery:

- Medicine packages should be stamped with bar codes (similar to the system used in India) that can be scanned at each point along the supply chain. To counteract counterfeits, this method would allow procurers to track the location of their purchases at any point.
- Pamphlets printed in local languages with correct dosage, usage, and storage information should be passed along the supply chain.
- Procurers should be transparent about their monitoring practices and list them prominently on their website

To help create incentives for manufacturers to produce high-quality medicines, procurers should patronize manufacturers who follow them.

❖ **Distributors:** International organizations and national governments often have problems managing the realities of substandard medicines on the ground. Distribution networks are vast and impossible to control completely, and distribution standards vary greatly. To increase distribution quality and uniformity, local actors should help monitor and spread awareness at the local level. These include non-governmental organizations and civil society groups interested in health care. Engaging these actors would help alleviate the information asymmetry problems mentioned in section 2.4.

To engage and empower such groups:

- Competitive grants and other sources of funding should be distributed through national governments, international organizations, and private grant-making foundations.
- Funding should be allotted to groups planning activities such as:
    - informing consumers about appropriate medicine dosage and usage;
    - awareness campaigns regarding the presence and problems of substandard and counterfeit medicines; and
    - publicizing resources available to consumers who want to report suspected substandards or counterfeits.

3. Clarify the definition of substandard medicines and increase emphasis on substandards

At the conceptual level, we identify two broad problems with how substandard medicines are treated internationally. First, little conceptual uniformity exists with respect to the definitions of substandard and

counterfeit medicines. Substandards and counterfeits require different solutions, so countries that do not differentiate between them often use a single solution to attack two very different problems. Second, substandard medicines have not received as much international attention as counterfeits.

To address the lack of conceptual uniformity, our goal is that the WHO's definitions of substandard medicines and of counterfeit medicines (see section 2.1) be universally accepted, because the WHO differentiates between the two types based on manufacturer. Also, as many non-governmental and international organizations and countries already use WHO tools, it seems suitable to use the organization's definition for substandard medicines.

Although we recognize that the WHO cannot require countries to adopt its definitions. To promote them, therefore, we recommend a two-step process.

- First, the WHO should convene a forum for all member states to discuss the importance of distinguishing between substandards and counterfeits. The forum could focus on determining and eliminating the factors that have prevented governments from adopting the definitions so far.
- Second, after the forum, the WHO and other organizations (national and international) involved in providing medical aid could create further incentives for governments to adopt WHO definitions. These could include requiring that they adopt agreed-upon definitions of substandard and counterfeit medicines before receiving medical aid.

To give more international attention to substandard medicines, we propose increased emphasis on substandards. Our recommendation that the WHO definitions of substandards and counterfeits be universally adopted should mitigate this problem at the national level. However, we find that researchers, who are key actors in the fight against the spread of substandards, also often emphasize counterfeits over substandards. As a result, there are few systematic data on substandard medicines separate from counterfeit medicines. To increase research on substandards we recommend that:

- The distinction between substandards and counterfeits be clarified for researchers and grant-making organizations at an international conference on the subject.
- The WHO and interested national governments fund competitive grants for researchers interested in studying the spread of substandards independent of counterfeits.[6]

[6] In a report on ensuring safe foods and medical products through stronger regulatory systems, the Institute of Medicine similarly recommends that the United States and other international actors increase investment in regulatory systems, in ways such as providing technical support for regulatory and surveillance systems in developing countries (Riviere and Buckley 2012, 3-9).

We recognize that the recommendations listed above are neither equally feasible nor of equally high priority. Table 2 delineates each recommendation based on feasibility and priority. To measure feasibility, we consider three factors: political feasibility, cost, and ease of implementation. High feasibility recommendations are those we judge to be politically feasible and relatively inexpensive and easy to implement. We categorize all other recommendations as "not immediately feasible." We recommend they be considered over the long term, however.

We determine priority based on the relative impact of recommendations to reduce the spread of substandard medicines. While we believe all our recommendations could improve the problem, we determine priority based on those we think will have a larger impact. Our categorization does not imply that lower priority recommendations be ignored, but rather that high priority recommendations be implemented first. We do not make any recommendations that are simultaneously of lower priority and not immediately feasible.

Table 2: Recommendations Categorized by Feasibility and Priority

	High Feasibility	Not Immediately Feasible
High Priority	- Researchers conduct ongoing, systematic research on best and worst manufacturers and countries - Governments and international organizations publish and frequently update lists of best and worst manufacturers - Manufacturers correctly label packages and communicate medicine usage information - Manufacturers and procurers include substandard or counterfeit reporting mechanisms on their websites - Manufacturers issue pamphlets printed in local languages with information on correct usage - Governments and international organizations fund research on substandards independent of counterfeits	- International organizations give aid to governments committed to improving regulatory and legal institutions - International organizations give aid to governments implementing citizen involvement projects - Procurers patronize manufacturers based on transparency - Procurers use monopsony power to patronize manufacturers based on the quality of their products - Manufacturers in developed countries increase competition - Manufacturers monitor and routinely test the quality of ingredients they buy - Manufacturers monitor medicines after they leave the point of production - All actors along supply chain check bar codes on medicines packages to track them - International organizations and governments give grants for non-state actors interested in local monitoring of substandard medicines - Foreign aid providers give aid to governments that use the WHO's definitions of "substandard" and "counterfeit"
Lower Priority	- Procurers use tools to create incentives for manufacturers to self-regulate. - Manufacturers and procurers increase transparency of processes on their websites - International organization holds conference to encourage standardization of definitions	NONE

Source: Authors

Appendix A: Medicines Quality Control

The following table summarizes the results of 33 studies of medicines quality control tests that informed our study of the prevalence of substandard medicines.

Table A1: Medicines Quality Control Testing Results

Countries Where Samples were Procured	Number of Samples	Findings (% of Samples which Are Substandard)	Country Where Samples were Manufactured	Types of Medicines Tested	Reference
Bangladesh	137	27%	NA	Various	Roy (1994) in Caudron et al. (2008)
17 unnamed countries in Africa	N/A	*Ingredient quality tests:* Ghana 14%, Nigeria 10%, Uganda 9%, Indian (small companies) 9%, Indian (large companies) 1%, Zambia 8%, Tanzania 7%, Kenya 7%, China 5%, Vietnam 5%, European Union 1%, Brazil 0%, Russia 0%, Switzerland 0%, United States 0% *Spectometry tests:* Ghana 19%, Uganda 17%, Zambia 17%, Nigeria 14%, Kenya 13%, Tanzania 13%, Vietnam 11%, Indian (small companies) 9%, Indian large companies 1%, Vietnam 8%, European Union 1%, Brazil 0%, Russia 0%, Switzerland 0%, United States 0%	Brazil, Ghana, Nigeria, Uganda, India, Zambia, Tanzania, Kenya, China, Vietnam, European Union, Russia, Switzerland, United States	Various	Bate et al. (2012)
Brazil, Ghana, Nigeria, Uganda, India, Zambia, Tanzania, Kenya, China, Vietnam, European Union, Russia, Switzerland, United States	N/A	%. Ingredient quality failures: Ghana 67%, Zimbabwe 57%, Mali 47%, Kenya 42%, Gabon 29%, Mozambique 20%, Sudan 5%. Dissolution test highest failures: Kenya 29%, Ghana 20%	Countries listed are countries of manufacture and not testing	Antimalarial: chloroquine tablets	Bate et al. (2012)
Cambodia	451	27%	Various	Antimalarial	Lon et al. (2006)
Cameroon, Madagascar, Chad	429	18%	N/A	Various	ReMeD (1995) in Caudron et al. (2008)

Countries Where Samples were Procured	Number of Samples	Findings (% of Samples which Are Substandard)	Country Where Samples were Manufactured	Types of Medicines Tested	Reference
Cameroon, Nigeria, Ghana, Tanzania, Kenya, Ethiopia	N/A	Nigeria 64%, Ghana 40%, Kenya 5%, Cameroon 37%, Tanzania 11%, Ethiopia 0%	N/A	Antimalarial	World Health Organization (2011)
China		Counterfeits rates as high as 66%	N/A	Various	Independent expert and activist Gao Jingde as reported in Bate and Porter (2009)
China	N/A	3%	N/A	Various	Government statistics as reported in Bate and Porter (2009)
China	almost 15,000	12%	N/A	Various	Shanghai Drug Administration Bureau, in Bate and Porter (2009)
China	N/A	<10%	N/A	Various	National Institute for the Control of Pharmaceutical and Biological Products, in Bate and Porter (2009)
Colombia, Estonia, India, Latvia, Russia, Vietnam	40	10%	N/A	Antituberculosis	Laserson et al. (2001) in Caudron et al. (2008)
Democratic Republic of the Congo	7	14%	Belgium	Antimalarial	Atemnkeng et al. (2007) in Caudron et al. (2008)
Gabon, Ghana, Kenya, Mali, Mozambique, Sudan, Zimbabwe	N/A	Highest failure rates: Mali 67%, Sudan 27%, Kenya 25%, Mozambique 25%	N/A	Antimalarial: chloroquine syrup	Maponga and Ondari (2003)
Ghana, Kenya, Nigeria, Rwanda, Tanzania, Uganda	N/A	Ghana 35%, Kenya 38%, Nigeria 32%, Rwanda 33% Tanzania 32%, Uganda 35%,	N/A	Antimalarial	Bate et al. (2008)
Two cities in and six cities in Africa	N/A	Delhi 12%, Chennai 5%, across six African cities 31%	India	Various	Bate et al. (2010)
Kenya	277	46%	Kenya	Various	Kibwage et al. (1992) in Caudron et al. (2008)
Kenya	102	31%	Imported	Various	Roy (1994) in Caudron et al. (2008)
Kenya	116	41%	N/A	Antimalarial	Amin et al. (2005) in Caudron et al. (2008)

Countries Where Samples were Procured	Number of Samples	Findings (% of Samples which Are Substandard)	Country Where Samples were Manufactured	Types of Medicines Tested	Reference
Kenya	N/A	42%	India/ China	Antimalarial	Atemnkeng et al. (2007) in Caudron et al. (2008)
Kenya	N/A	40%	N/A	Antimalarial	Nsimba (2008)
Laos	366	46%	Laos/ Thailand	Ampicillin, tetracycline, chloroquine, acetylsalicylic acid	Stenson et al. (1998) in Caudron et al. (2008)
Laos	300	22%	N/A	Ampicillin tetracycline, chloroquine, acetylsalicylic acid	Syhakhang et al. (2004) in Caudron et al. (2008)
Myanmar	212	16%	Various	Various	Wondemagegnehu (1999) in Caudron et al. (2008)
Myanmar, Thailand, Vietnam	N/A	Thailand 9%, Vietnam 8%, Myanmar 16%	N/A	Various	Frankish (2003)
Nigeria	581	48%	Various	Various	Taylor et al. (2001) in Caudron et al. (2008)
Nigeria	81	36%	N/A	Various	Shakoor et al. (1997)
Nigeria	N/A	50%	40% of failures appear to be produced in India.	Various	Shakoor et al. (1997)
Nigeria, Thailand	96	40%	N/A	Antimalarial, antibacterial	Shakoor et al. (1997)
Tanzania	33	36%	Cyprus, Tanzania, India	Antimalarial	Minzi et al. (2003) in Caudron et al. (2008)
Thailand	15	40%	N/A	Various	Shakoor et al. (1997)

Countries Where Samples were Procured	Number of Samples	Findings (% of Samples which Are Substandard)	Country Where Samples were Manufactured	Types of Medicines Tested	Reference
Thailand	N/A	9%	N/A	Various	Morris and Stevens (2006)
Vietnam	288	8%	Various	Various	Wondemagegnehu (1999) in Caudron et al. (2008)

Sources: see Reference column Notes: Bate et al. (2012): Medicines found to be counterfeit by visual test were removed prior to quality testing.

Appendix B: U.S. Pharmacopeial Convention: "Manufacturers of Substandard Medicines"

Based on data retrieved from the U.S. Pharmacopeial Convention (USP) website Medicines Quality Database, this appendix discusses manufacturers of samples found to be substandard. It represents an overview of the major manufacturers of substandard medicines and shows in which countries these medicines were found. The database allowed us to narrow our study of major consumer and manufacturer countries of substandard medicines.

The USP Medicines Quality Database provides technical assistance to strengthen medicine quality assurance and quality control systems in priority countries for the U.S. Agency for International Development (USAID) projects. Starting in Asia in the early 2000s, medicine samples have been collected and examined as a part of the Drug Quality and Information program. The USP and the USAID have expanded the database and have made it more globally applicable by adding samples from Africa and South America. After the establishment of Promoting the Quality of Medicines program in 2009, the database evolved into a project under this program. As one of the USAID's main goals is to support the distribution of antimalarial, antiretroviral, and antituberculosis medicines in developing countries, the database was a useful tool in our research and aligned well with our project's focus on the substandard medicine supply chain in developing countries (U.S. Pharmacopeial Convention n.d.).

The Medicines Quality Database contains information on medicines received from collection and examination of medicine samples from various countries within Asia, Africa, and South America. These samples were collected from various points including the public sector (which includes government institutions and faith-based organizations), the private sector (licensed establishments), and informal sectors (consisting of unregulated establishments and vendors operating without a license to sell medicines) (U.S. Pharmacopeial Convention n.d.).

This database focuses on medicines that are relevant to national health programs in the USAID priority countries. Most of the medicines are used for the treatment of endemic diseases such as malaria, HIV/AIDS, and tuberculosis. After the collection of medicine samples, most were screened by the staff of the program using basic tests or by the country's official medicine control laboratory for verification and confirmation testing. Any samples are defined as a substandard when they fail quality testing. In other words, they do not follow the standard set according to the methodology used (U.S. Pharmacopeial Convention n.d.).

We retrieved all medicine data from the Medicines Quality Database, which was accessible for non-commercial extrapolation. We downloaded information regarding the name of manufacturer, therapeutic indication, active pharmaceutical ingredients, country where the medicine was collected, year of collection, and test results (U.S. Pharmacopeial Convention n.d.).

After we retrieved information on more than 4,500 samples of antimalarial, antituberculosis, and antiretroviral medicine from Asia, Africa, and South America, we created a spreadsheet and grouped medicine samples by name of manufacturer. We summed the total of all medicine samples that were claimed as products of each manufacturer. After that, we counted the numbers of substandard samples were counted and determined the percentage of the substandard samples for each manufacturer. Google and MediLexicon were used to obtain the country location for each manufacturer (MediLexicon International Ltd. n.d.). Results are summarized in Table B1.

Table B1 lists manufacturers' names in order of the highest percentage of substandard medicine to the lowest prevalence of substandard medicines. Also, those names are separated by region. According to Table B1, countries where substandard medicine manufacturing occurs include India, China, Thailand, Vietnam, the United Kingdom, the United States, Portugal, Cambodia, the Philippines, Guyana, Kenya, El Salvador, Chile, Belgium, and Switzerland. We decided to not include manufacturers where less than five samples were taken. The results show that the key countries with manufacturers responsible for substandard production in Asia are China, India, Vietnam, and Thailand. The key countries responsible for substandard production in South America and Africa are Guyana and Kenya. Almost all key manufacturer countries are located in the region that they are responsible for, although China and India have key manufacturers that export to Africa.

The key victims or recipients of substandard medicine in Asia are Cambodia, the Philippines, Vietnam, and Laos. The South American victim is Guyana; whereas the African victim is Kenya (Table B1). Among the three therapeutic indicators, antimalarial medicines are the most concerned substandard medicine problem in Asia and the only problem in South America and Africa.

The Medicines Quality Database has four main limitations. The first is that it is not the most ideal representation of the developing world. This database is tailored for the USAID projects whose target countries do not include all developing countries. Therefore, most medicine samples in this database were picked from the USAID priority countries. The sampled countries were Ghana, Kenya, Columbia, Ecuador, Peru, Guyana, Cambodia, Laos, Vietnam, and the Philippines.

The second limitation is that not every manufacturer's country can be traced. Names of manufacturers are the only clue about each manufacturer that the database gives. Some names, such as KPN, are too common to identify which companies they are. Some names, such as CREMY, could not be located after an extensive internet search.

The third limitation is that manufacturers are not always responsible for substandard medicines. Substandard medicines do not necessarily come from manufacturer

errors. Medicines can become substandard due to poor conditions during procurement, distribution, and storage (U.S. Pharmacopeial Convention n.d.).

Finally, only a few samples of medicines were collected for some manufacturers. A high percentage of substandard sample cannot lead us to the conclusion that one manufacturer is the key substandard medicine producer, given that only a few medicines were sampled. We can only conclude that a manufacturer is a key producer if a high percentage of substandard samples occur together with a large number of collected total samples.

Table B1: Percentage of Substandard Medicines by Manufacturer

Manufacturer	Medication	Country of Manufacture	Total Samples[a]	Percentage of Substandard Medicines[b]	Countries Where Consumed[c]
Asia					
Master Pharmaceutical Part.	Antimalarial	Not found	2	100	Cambodia
Laos	Antimalarial	Not found	1	100	Vietnam
UKP Pharma	Antimalarial	Not found	1	100	Cambodia
VKP Pharmaceutical	Antimalarial	India	1	100	Cambodia
Brainy Pharmaceutical	Antimalarial	Thailand	99	85	Cambodia
GP Pharma Ltd.	Antimalarial	United Kingdom	3	67	Cambodia
CREMY	Antimalarial	Not found	2	50	Laos
Cuu Long Pharmaceutical Joint-Stock Co.	Antimalarial	Vietnam	2	50	Vietnam
National Pharmaceutical Joint-Stock No 25	Antimalarial	Vietnam	2	50	Vietnam
Tipharco	Antimalarial	Vietnam	2	50	Vietnam
United Laboratories, Inc.	Antituberculosis	United States	7	43	Philippines
National Pharmaceutical Joint-Stock No 2	Antimalarial	Vietnam	3	33	Vietnam
Specia	Antimalarial	Not found	3	33	Vietnam
Gateway Pharmaceuticals	Antimalarial	Not found	7	29	Cambodia
Interphil Laboratories	Antituberculosis	Many locations	17	18	Philippines
Masa Lab Co., Ltd.	Antimalarial	Thailand	18	17	Cambodia
Quang Binh Pharmaceutical Joint-Stock Co.	Antimalarial	Vietnam	6	17	Vietnam
Pharmaceutical-Medicine Instrument Company Thanh Hoa	Antimalarial	Vietnam	7	14	Vietnam
Vidipha Pharmaceutical Joint-Stock Co.	Antimalarial	Vietnam	7	14	Vietnam
National Pharmaceutical company No 3	Antimalarial	Vietnam	15	13	Vietnam
Chemephand Medical	Antimalarial	Thailand	9	11	Cambodia
Thanh Hoa Medical Materials Pharmaceutical Co., Ltd.	Antimalarial	Vietnam	9	11	Vietnam
Kunming Pharmaceutical factory	Antimalarial	China	12	8	Laos
Factory No: 3	Antimalarial	Not found	14	7	Laos
Utopian Co., Ltd.	Antimalarial	Thailand	71	4	Cambodia
Mepha Ltd.	Antimalarial	Portugal	28	4	Cambodia

Manufacturer	Medication	Country of Manufacture	Total Samples[a]	Percentage of Substandard Medicines[b]	Countries Where Consumed[c]
Asia					
Lloyd Laboratories, Inc.	Antituberculosis	Many locations	29	3	Philippines
Medical Supply Pharmaceutical Enterprise	Antituberculosis	Cambodia	29	3.45	Cambodia
Scheele Laboratories Phil., Inc.	Antituberculosis	Philippines	32	3.13	Philippines
Amherst Laboratories, Inc.	Antituberculosis	Not found	36	2.78	Philippines
Cipla Ltd.	Antiretroviral	India	46	2.17	Cambodia
Mekophar Chemical Pharmaceutical Joint-Stock Co.	Antituberculosis, Antimalarial	Vietnam	478	2.09	Vietnam, Laos
KPN	Antimalarial	Not found	67	1.49	Laos
Nam Ha Pharmaceutical Joint-Stock Co.	Antimalarial	Vietnam	182	0.55	Vietnam
South America					
New GPC Farm	Antimalarial	Guyana	49	4.08	Guyana
Africa					
Comet Healthcare Ltd.	Antimalarial	Kenya	2	100.00	Kenya
NBSW Pharma Ltd.	Antimalarial	Not found	2	100.00	Kenya
Farmaceuticos L. Sadecv	Antimalarial	El Salvador	1	100.00	Kenya
Gesto Pharmaceuticals Ltd.	Antimalarial	Kenya	1	100.00	Kenya
Mepro Pharmaceuticals PVT Ltd.	Antimalarial	Chile	1	100.00	Kenya
MVF BV for Dafra Pharma	Antimalarial	Belgium	1	100.00	Kenya
Umedica Laboratories Pvt Ltd.	Antimalarial	India	1	100.00	Kenya
Urnav B.V.	Antimalarial	Kenya	1	100.00	Kenya
Bliss Gvis Pharma Ltd.	Antimalarial	India	27	7.41	Kenya
Laboratory & Allied Ltd.	Antimalarial	Kenya	18	5.56	Kenya
Cosmos Ltd.	Antimalarial	Kenya	38	2.63	Kenya
Ajanta Pharma Limited	Antimalarial	India	60	1.67	Kenya
Novartis	Antimalarial	Switzerland	83	1.20	Kenya

Sources: Authors, based on data from U.S. Pharmacopeial Convention (n.d.)

[a] Total drug samples obtained from each manufacturer

[b] Percentage of substandard medicines samples out of total number of samples

[c] Countries in which substandard medicines samples were found

Note: The unknown manufacturers whose samples are included in the Medicines Quality Database make up 11 percent of substandard samples in Asia and 15 percent in Africa.

Appendix C: Fortune 500 Pharmaceutical Companies

We looked at whether Fortune 500 pharmaceutical companies have explicit information on their efforts to combat substandard medicines on their websites. The following table compiles this information.

Table C1: Publicly Displayed Information on Counterfeit Tracking and Supply Chain Monitoring on Pharmaceutical Company Webpages

Company	Global 500 rank	Revenue in $US Billions	Counterfeit Tracking	Supply Chain Standards/ Monitoring	Notes
Johnson & Johnson	103	64	Yes	Yes	
Pfizer	152	48	Yes	No	Counterfeit information is for U.S. customers only
GlaxoSmithKline	168	45	Yes	Yes	
Roche Group	171	42	Yes	No	Specifically mentions counterfeit monitoring as a government responsibility
Sanofl-Aventis	181	42	No	Yes	
Novartis	183	41	Yes	No	Assumes some responsibility for tracking, seizing and destroying counterfeit product
AstraZeneca	268	32	Yes	Yes	
Abbott Laboratories	294	30	Yes	Yes	
Merck	378	24	Yes	No	
Wyeth	401	23	N/A	N/A	Wyeth is now owned by Pfizer
Bristol-Myers Squibb	435	21	Yes	No	
Eli Lilly	455	20	Yes	No	

Sources: CNN Money (2009), company websites

Appendix D: Regulatory and Enforcement Structures

The following section compares regulatory and enforcement mechanisms (Table D1) and weaknesses in regulatory regimes, efforts to combat substandard medicines, and proposed solutions in each country (Table D2).

Table D1: Comparison of the Structure of Regulatory and Enforcement Structures in China, India, Nigeria, Ghana, Kenya, and Thailand

	China	India	Nigeria	Ghana	Kenya	Thailand
Major Regulatory Agencies	State Food and Drug Administration (SFDA)	Central Drugs Standard Control Organization (CDSCO)	National Agency for Food and Drug Administration and Control (NAFDAC)	Food and Drugs Board (FDB)	Pharmacy and Poisons Board	Food and Drug Administration (FDA)
Formulation of Regulatory Standards	SFDA	Central government	NAFDAC Regulation and Regulatory Affairs Directorate, in consultation with the legal unit	National Drugs Programme, Ministry of Health, in accordance with national legislation. Additional guidelines issued by the FDB	Pharmacy and Poisons Board	FDA
Manufacturing Licensure	SFDA	CDSCO and state-level agencies, depending on type of medicine	NAFDAC	FDB	Pharmacy and Poisons Board	FDA under the recommendation of the Drug Board
Registration of Medicines	SFDA	CDSCO	NAFDAC Regulation and Regulatory Affairs Directorate	FDB, Drug Evaluation and Registration Department	Pharmacy and Poisons Board	FDA under the recommendation of the Drug Board

	China	India	Nigeria	Ghana	Kenya	Thailand
Regulation of Manufacture, Sale, and Distribution of Medicines	-Manufacture: Regulatory departments at or above the provincial level -Sale and distribution: Regulatory authorities at all levels: central, provincial, autonomous region, and municipality	State-level agencies	NAFDAC Regulation and Regulatory Affairs Directorate	FDB regional offices	Pharmacy and Poisons Board	The Drug Control Division (Bangkok and its territories) and provincial public health offices (other provinces)
Inspection of Medicines	Regulatory authorities at all levels	State-level agencies	NAFDAC Establishment Inspection Directorate and Ports Inspection Directorate	FDB Drug Inspectorate Department at regional offices	Ministry of Medicines (MOMS) Post Market Surveillance, Department of Pharmacovigilance, Pharmaceutical Inspectorate Department	FDA and Drug Analysis Division of the Medical Science Department
Quality Assurance	Regulatory authorities at all levels	State-level agencies	NAFDAC Laboratory Service Directorate	FDB	MOMS	FDA
Punishment of Infractions	SDFA	Judicial system	NAFDAC Enforcement Directorate	FDB regional offices	Pharmaceutical Inspectorate	FDA

	China	India	Nigeria	Ghana	Kenya	Thailand
Important Legislation Regarding Medicines	- Drug Administration law, 2001 - Drug Regulations and Legislation, 2002 - Measures on the Administration of Drug Registration, 2002 - Measures on Administration and of Reporting and Monitoring of Adverse Drug Reactions, 2004	- The Drug and Cosmetics Act, 1940 - The Pharmacy Act, 1948 - Good Clinical Practice guidelines, 2002	- Decree No. 15, 1993, amended by Decree No. 20, 1999: establishes the NAFDAC - Drugs and Related Products Decree No. 19, 1993, amended by Decree No. 20, 1999: mandates regulated products' registration - Counterfeit/Fake Drugs/Unwholesome Processed Foods Decree No. 25, 1999, and Drugs and Related Products Decree No. 19, 1993: establish the concept of substandard products	- Food and Drugs Act, 1992: establishes FDB - Pharmacy Act 489, 1994: establishes the Pharmacy Council - Public Procurement Act 663, 2003	- Pharmacy and Poisons Act (1957) - Kenya National Drug Policy (1994)	The Drug Act 1967, revised in 1987

Sources: Authors. Based on data from State Food and Drug Administration of China (n.d.), Torstensson and Pugatch (2010), Bate and Porter (2009), Central Drugs Standard Control Organization of India (2009, n.d.a, n.d.b, n.d.c), Partnership for Safe Medicines India (n.d.), Ghana Legal Environmental Information (n.d.), Ghana Food and Drugs Board (n.d.a, n.d.b, n.d.c, n.d.d. n.d.e., n.d.f.), GhanaWeb (2011), Ghana Ministry of Health (2004, 2011), Global Health Consulting Group (2009), National Drugs Programme (2009), Ghana Business New (2012), Nigeria Federal Ministry of Health (2011), NAFDAC Nigeria (n.d.a., n.d.b, n.d.c., n.d.d., n.d.e., n.d.f.), Nigerian Food and Drug Regulatory Advisor (2010a, 2010c), Ugwoke (2012), World Health Organization (2011), Garuba et al. (2009), Luoma et al. (2010), Thai Food and Drug Administration (1999, 2008, n.d.), Thai Drug Watch (2011), and Sukin (2007).

Table D2: Assessment of Regulatory and Enforcement Mechanisms in China, India, Nigeria, Ghana, Kenya, and Thailand

Country	Weaknesses in Regulatory Regime	Efforts to Combat Substandard Medicines	Authors' Proposed Policy Responses
China	- Continued substandard production - Inconsistent enforcement - Counterfeiting big issue, counterfeiters not subject to regulation - Government and local corruption - Lack of accountability and oversight	- Strengthened State Drug and Food Administration - Pharmacovigilance network for reports of adverse drug reactions - Increased penalties for substandards and counterfeits - Execution of ex-food and drug chief	- Better implementation of existing regulations - Increased emphasis on enforcement - Increased penalties for corruption - Career-based incentives for local level leaders to regulate effectively - Regulate drug manufacturing and chemical manufacturing
India	- Lack of comprehensive system of regulation - Definitions of substandards and counterfeits differ from the WHO - Regional disparities in regulation and enforcement - Inadequate testing facilities - Lack of infrastructure for monitoring and enforcement - Slow judicial processes - Minimal penalties for producing substandards	- Reward scheme for whistleblowers - Barcodes required for all drugs - Increased vigilance on exported drugs	- Creation of administrative offices to strengthen port offices, zonal offices, and testing laboratories - Infrastructure improvement to enhance Central Drugs Standard Control Organization (CDSCO) functioning - Creation of National Drug Authority - Establishment of state-level intelligence and legal organizations - Incentives for local officials to regulate effectively through non-governmental organizations and media
Thailand	- Outdated drug advertising control and monitoring legislation - Agencies monitoring medicines storage and transportation do not function well. - Low level of cooperation among related agencies on substandard medicine prevention and suppression	- Good Manufacturing Practice certificate: quality control of medicine during manufacturing - Medicines Quality Assurance Project (2006-2008): assure the quality of drugs for domestic consumption	- Drug list revision: include the solubility standard of medicines' active ingredients - Single Window: increase drug information accessibility for related public agencies - Enter ministerial regulation on Good Pharmacy Practice into force: medicine's quality control during storage at pharmacies - Promote public on and contribution in drug quality control and monitoring

Country	Weaknesses in Regulatory Regime	Efforts to Combat Substandard Medicines	Authors' Proposed Policy Responses
Nigeria	- Enforcement weak due to low human capital, decentralized supply chain, and corruption - Lack of transparency enables corruption and low compliance	- 2001: organizational restructuring, reforms improve regulation and public awareness - Stronger relationships with China and India - 2010: product and document verification system	- Establish and enforce conflict of interest guidelines - Publish internal/external audits for agency positions - Improve staff training and material resources - Regain access to ports with agreement with Ports Authority - Produce good practice guidelines for suppliers
Ghana	- Lack of political will to appropriately regulate - Lack of professionalism in Food and Drug Board staff due to poor training and lack of punishment for infractions or low quality work - Insufficient funds dedicated to provide material resources to inspect and run laboratory quality checks - Result in lack of enforcement of regulations - Lack of enforcement leads to low compliance, prevalence of substandard medicines	- Establishment of the National Drugs Programme and the National Drug Policy - Creation of the National Essential Drugs List and Standard Treatment Guidelines - Placement of regional experts to teach how to use medicines and train pharmacists	- Educate public about medicine quality issues - Food and Drug Board leadership should better train staff and punish infractions for low quality work, to improve enforcement of regulations - Increase staff and equipment for increased monitoring at all stages of supply chain - If necessary, international community should create incentives for these changes through foreign direct investment commitments conditional on improvements
Kenya	- Inadequate legal framework - Conflicting responsibilities - Outdated registration procedures	- Essential Medicines List - Inspections and lab testing by Ministry of Medicines (MOMS) and the Department of Pharmacovigilance	- Update regulatory framework - Consolidate regulations and licensure - Address gaps in laws

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