Poor Quality Drugs and Global Trade: A Pilot Study

Roger Bate, AEI

Ginger Zhe Jin, University of Maryland and NBER

Aparna Mathur, AEI

Amir Attaran, University of Ottawa

Abstract

Experts claim that some Indian drug manufacturers cut corners and make substandard drugs for markets with non-existent, under-developed or emerging regulatory oversight, notably Africa. This paper assesses the quality of 1470 antibiotic and tuberculosis drug samples in solid oral form (tablet or capsule) that claim to be made in India and were sold in Africa, India, and five mid-income non-African countries. We find that 10.9% of those products fail a basic assessment of active pharmaceutical ingredients (API), and the majority of the failures are substandard (7%) as they contain some correct API but the amount of API is under-dosed. The distribution of these substandard products is not random: they are more likely to be found as unregistered products in Africa than in India or non-African countries. Moreover, our finding is robust for manufacturer-drug fixed effects, and is unlikely to be explained by differences in storage conditions as the five Indian cities in our sample are on average more likely to have high temperatures, above 25°C or 30°C, than the other African or non-African cities. A more likely explanation is that Indian pharmaceutical firms and/or their export intermediaries differentiate drug quality according to the destination of consumption.

Keywords: prescription drug, quality, international trade, Africa, India.

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Contact Information: Roger Bate: American Enterprise Institute, 1150 17th St NW, Washington DC 20036, 202-828-6029,rbate@aei.org. Ginger Zhe Jin: 3115 F Tydings Hall, Department of Economics, University of Maryland, College Park MD 20742, (301) 405-3484, jin@econ.umd.edu. Aparna Mathur: American Enterprise Institute, 1150 17th St NW, Washington DC 20036, 202-828-6026, amathur@aei.org. Amir Attaran: Faculty of Law, Institute of Population Health, University of Ottawa, 57 Louis Pasteur St, Ottawa, Ontario, K1N 6N5, 613-562-5800, aattaran@uOttawa.ca.

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I. Introduction

Free trade allows specialization, encourages competition and generally enhances efficiency. However, when it comes to heavily regulated products such as prescription drugs, globalization implies a patchwork of uneven regulations. Countries differ greatly in their product registration process, quality standards, price controls, customs and law enforcement. For a drug to be produced in country A and exported to country B, legitimate manufacturers have to meet multiple regulatory targets in both countries, which increases the cost of compliance while introducing incentives for cheating and even trading falsified or substandard medicines.

In this paper, we examine 1470 samples of antibiotics and tuberculosis (TB) medicines claiming to be made in India. They were collected from five cities inside India as well as 17 low-to-middle-income countries outside of India, and tested for basic quality using the Minilab protocol. We find that a significantly higher fraction of these Indian-made drugs are of poorer quality if they were purchased from Africa than from India or from Non-African mid-income countries such as China, Brazil, Turkey, Thailand and Russia. These patterns persist even after we control for manufacturer-drug fixed effects, suggesting that they are driven by variations within the same manufacturer as labeled on the package. Moreover, the above pattern is driven more by non-registered substandard products that contain insufficient active pharmaceutical ingredient (API) than by falsified drugs that contain zero API.

Pharmaceutical experts anecdotally have observed that some Indian manufacturers sell inferior medicines to markets where drug regulatory oversight is weak, and better medicines to markets where oversight is more effective.[1] This paper attempts to test whether this perception is validated by the data. In doing so, there are some challenging factual confounders: isolated reports[2], now several years old, indicate Chinese organized criminals counterfeited Indian drugs; and even genuine, top quality Indian drugs can degrade with improper handling so as to become

1 On May 13, 2013, Ranbaxy Laboratories Limited, a major Indian drug manufacturer, pleaded guilty with seven US federal criminal charges on selling adulterated generic drugs, fabricating data, and committing fraud. The company was reported to have a culture that was "for management to dictate the results it wanted and for those beneath to bend the process to achieve it." Dinesh Thakur, the whistle blower, described "how Ranbaxy took its greatest liberties in markets where regulation was weakest and the risk of discovery was lowest." (Fortune, May 15, 2013 "Dirty Medicine" by Katherine Eban, accessed at http://fortune.com/2013/05/15/dirty-medicine/ on August 27, 2014). See also Ranbaxy Writ Petition, Supreme Court of India, 2013, accessed at http://www.scribd.com/doc/160520772/149915683-Ranbaxy-Writ-Petition on August 27, 2014.

2 http://timesofindia.indiatimes.com/business/india-business/Chinese-passing-off-fake-drugs-as-Made-in-India/articleshow/4633377.cms

substandard. Neither of these circumstances is the fault of Indian companies. However, our findings suggest that the main problem for inferior quality in Africa of Indian products is more likely in the manufacturing or distribution than in counterfeiting or careless storage at the purchase city. One likely explanation is that some Indian manufacturers as labeled in our drug samples and/or their export intermediaries differentially supply poor quality products to African markets where GDP per capita is low and local regulations are weak. This could be driven by economic concerns: because demand conditions vary across countries, suppliers may have incentives to deliver lower-quality products to a low-end market or conduct less quality control in such a market.

We review the related literature in Section 2 and then describe how we arrive at the above data patterns in Section 3. Section 4 explores a few potential explanations. While it is often difficult to pin down the intent of organized crime, we crosschecked our samples with their product registration status at the destination country, as failure to register a medicine is unlawful in most countries and *prima facie* evidence of wrongdoing. We argue that the significant cost of product registration affects the incentive of quality choice by manufacturers. Section 5 discusses the implication of our findings for various parties.

II. Literature

Our work is related to two strands of literature: one on drug quality in global markets, the other on international trade of medicines and other merchandise.

The literature on global drug quality aims to document the extent of quality problems. As summarized in IOM (2013), industrial databases, international police investigations, case studies, news reports, and scientific works based on retail drug samples have all pointed to a persistent and probably growing[3] problem of falsified and substandard drugs[4]. However, existing evidence

[3] We are addressing substantive quality problems in medicines that do not help the patient in addressing the disease, not those that exhibit simply superficial concerns. For example, some medicine could be rejected by health authorities because tablets (or even just the packaging) may be discolored, when in fact the medicine may work perfectly well.

[4] Most studies focus on a few specific countries or a few specific products, making it difficult to compare across studies. Due to data, budget and institutional limitations, many studies rely on convenience sampling rather than probability-based sampling, and draw more samples from formal retail channels (e.g. pharmacy stores) than from informal channels (e.g. street vendors or bus vendors). One exception is Kaur et al. (2008), who used stratification to collect 1,080 antimalarial drug samples from Tanzania in 2005 and found a failure rate of 12.2% after testing 301 samples. In another example, Stanton et al. (2012) randomly chose 75 vendors in Ghana and from them collected 101 samples of ergometrine and oxytocin (drugs used to treat postpartum hemorrhage). They found that 89% failed

often suffers from reporting bias, a small number of observations, and lack of representative coverage. As a result, public data are limited in estimating the magnitude of the problem. That being said, data from the Pharmaceutical Security Institute indicate that poor-quality medicines were found in 124 countries in 2011, with the problem severer in low- and mid-income countries than in developed countries (IOM 2013). One potential explanation is that developing countries often have weak regulatory oversight and lax law enforcement, which attract the manufacture and trade of poor-quality drugs.

The international trade literature has long been interested in how product quality varies by origin, destination, and as compared to domestic trade. However, product quality is often difficult to measure, leading most researchers to rely on price as a proxy for quality (Schott 2004; Hummels and Skiba 2004; Hummels and Klenow 2005; Hallak 2006; Khandelwal 2010; Baldwin and Harrigan 2011; Johnson 2012; Crozet, Head and Mayer 2012). As detailed in our earlier studies, price is at best a noisy signal of drug quality in the global market (Bate, Jin and Mathur 2010) and sometimes can be misleading as counterfeiters mimic legitimate drugs in packaging and price (Bate, Jin and Mathur 2014).

A strand of the trade literature focuses on medicine, but mostly on patent protection rather than drug quality. Using the implementation deadline of the World Trade Organizations Trade-related Intellectual Property Rights (TRIPS), researchers have shown that patent protection led to faster market launch, higher sales, and increased prices for innovator-branded drugs (Kyle and Qian 2013; Duggan and Goyal 2012).[5] Better patent protection is also found to encourage drug innovation and patent applications (Arora et al. 2008, Kyle & McGahan 2012) but may reduce consumer welfare (Chaudhuri, Goldberg and Jia 2006).

Little academic work has looked at the trade of cheaper and potentially poorer-quality drugs in global markets. Our pilot study aims to address this gap in the literature. In particular, we focus on generic antibiotics and tuberculosis (TB) medicines that are labeled "made in India." In the past two decades, India has grown to be the third largest manufacturing country for pharmaceuticals, accounting for 13% of the global pharmaceutical production (in value) and

pharmacopeial testing and only 0% of ergometrine and 26% for oxytocin met pharmacopeial specifications.

[5] Similar to patent protection, other pharmaceutical regulations may affect the diffusion of new drugs as well. For example, Cockburn, Lanjouw and Schankerman (2014) show that stringent price control tends to delay new drug launches in both low- and mid-income countries.

22% of international trade in generic medicines (Sharma, Kumar and Sharma 2008; KPMG 2006).[6]

One primary advantage of Indian-made drugs is that they tend to be low priced (Cameron et al. 2008). Health Action International's interactive map shows that Indian generic ciprofloxacin is the cheapest in the world, often by two orders of magnitude from richer market innovator versions (HAI 2010). Despite the price advantage, USP (2013) and Stanton et al. (2014) have published evidence of frequent, often serious quality failures in "made in India" medicines (purchased in and out of India), which paints a more bleak picture than what the Indian government admitted in its 2009 report (CDSCO 2009).

We choose to focus on common broad-spectrum antibiotics and specialized tuberculosis antibiotics in solid oral form (tablets and capsules), partly because these anti-bacterial medicines are among the most commonly used in developing countries[7], and because they are relatively cheap making it possible to purchase and test a large sample . Inferior versions of antibiotics can be both fatal to the patient, and promote drug resistance that undermines the future effectiveness of even good quality medicines. Anti-infectives are also thought to be one of the drug categories most affected by poor drug quality (IOM 2013).

Not only will inferior medicines harm individual patients, but intermittently effective medicines containing some but not sufficient anti-bacterial ingredients can also evolve drug resistance (Bate et al 2013, Binagwaho et al 2013). Experience teaches that drug resistance does not stay confined, but spreads to other countries. Thus poor quality medicines consumed in poor countries can evolve resistance that diminishes from treatment outcomes even in rich countries where good quality medicines predominate.

III. Data Description

[6] Thousands of pharmaceutical companies operate in India, some are large and licensed while others are small and informal (KPMG 2006). According to an Indian government report on the industry (MCFDP 2012), nineteen of the twenty-one large Indian pharmaceutical manufacturers devoted at least 50% of their net sales to export in 2010-11, of which eight exported more than 75%.(Based on authors' calculation from Table 2 of MCFDP (2012), Section 2.9, page 16.)

[7] We choose not to include antimalarial drugs because there is so little malaria in some locations that availability of medicines to treat it is highly limited. We also exclude vaccines such as BCG because it is not deployed routinely in many of the locations we sampled from.

Over 2,500 treatments of ciprofloxacin, erythromycin, isoniazid and rifampicin, were collected from pharmacies in 22 cities of 18 low- to mid-income countries between 2009 and 2012. The sampling methodology is detailed elsewhere (Bate et al 2014). Briefly, in each target city, we instructed covert shoppers from the local population to randomly walk into pharmacies and claim that a family member needed a specific type of drug. To mimic real patients as much as possible, the covert shoppers did not present a doctor's prescription and always purchased the pharmacist-suggested brand. Informal drug vendors (bus vendors, mobile carts, etc.) are prevalent in some locations, but to be able to compare across all locations, our shoppers only visited pharmacies with a regular storefront. As a result, our samples are likely to understate the problem of poor-quality drugs, given the expectation and existing evidence that informal vendors sell worse drugs (IOM 2013).

All medicines were assessed following the Global Pharma Health Fund (GPHF) e.V. Minilab® protocol to identify substandard or counterfeit medicines. The key test for our sample is the semi-quantitative thin-layer chromatography (TLC), which assesses the presence and concentration of active ingredient in a test sample as compared to the reference standard.[8] Given the size of our sample and funding constraints, TLC is the best test method we can afford.[9] It is important to note that passing the TLC test is a *necessary condition for the medicine to work, but it is far from sufficient.* To be sure of the quality of a medicine, one would need to conduct many tests with more advanced (and expensive) laboratory and clinical methods to detect dissolution time, impurities, degradation products, provenance and bioequivalence. In that sense, our estimation of quality is a very basic one, which understates the frequency of quality failures. This is why we title the paper as a pilot study. Organizations with larger budgets should undertake more definitive tests to assess how many more, and which types of, products fail more comprehensive analyses.

All tests were conducted within 60 days after purchase in the Africa Fighting Malaria Minilab in Cambridge, UK. Following the classification in Bate, Jin and Mathur (2014), a drug

[8] The TLC test requires the tested product to have 80-100% of the correct active ingredient, when compared to the reference standard. The principal spot obtained with the test solution should travel the same distance on a TLC plate and yield highly similar shapes, colors, intensities, and sizes as the reference standard. The distance that the sample travels informs of the drug identity; the intensity of the spot informs of the amount of active ingredient (Jähnke et al. 2001).

[9] TLC test has strengths and drawbacks as compared to more advanced techniques such as high-performance liquid chromatography (HPLC) and spectroscopy (IOM 2013). Its main strength is the ability to yield "versatile and robust" results at a low cost (Kaale et al., 2011).

sample is referred to as falsified if it contains zero correct API[10], and referred to as substandard if it contains some correct API but the amount of API is under-dosed (below 80%).

As acknowledged in other studies (Attaran et al 2012), the legal distinction between falsified and substandard products is one of intention: both sorts of compromised medicines are not as labeled and violate the relevant technical or regulatory standards, but substandard medicines are compromised accidentally or negligently, while falsified medicines are compromised intentionally, with this difference not always being apparent from the content of the medicine. In other words, legally speaking, falsified products are the product of organized criminal intent, but substandard medicines could be wrongfully produced by otherwise legitimate, law-abiding manufacturers. While criminal intent may not always be apparent from a chemical analysis , this paper distinguishes substandard and falsified drugs by API only.

The API results on ciprofloxacin, isoniazid and rifampicin have been reported in several peer reviewed papers (Bate, Jin, Mathur 2011; Bate et al. 2013; Bate, Jin, Mathur 2014) but none of them compares drug quality of the same manufacturer across different purchase countries. The data on erythromycin are used for the first time in this paper.

Our sample contained medicines from 29 countries of manufacture as stated on the packaging, among which India is the largest. No other manufacture country has similar presence in our sample that would facilitate a meaningful, statistical comparison against India. For this reason, we focus here only on the 1470 products that claim to be "made in India". The label of these products reveals 17 unique Indian manufacturers.[11] Note that being labeled "made in India" does not necessarily mean the actual manufacturer is an Indian firm. In eight samples of ciprofloxacin, we have learned that the products were counterfeits made in or shipped from China, based on information from the companies in question, who we asked for confirmation.[12] In Section 4, we will explore counterfeiting as a potential explanation for our quality test results and check the robustness of data analysis excluding these eight counterfeiting cases.

Table 1 shows the distribution of drugs by drug type and purchase country. Among the four drug types, ciprofloxacin and erythromycin are mainstream broad-spectrum antibiotics,

[10] Only a few samples have obvious falsified packaging and they all turn out to have zero API.

[11] Our IRB commitment prevents us from revealing the identity of individual manufacturers as labeled on the package.

[12] In Bate, Jin and Mathur (2014), we coded these eight cases as manufactured in China, thus the number of India-made ciprofloxacin is 683 instead of 691 in that paper. We keep these 8 cases here because the analysis sample of this paper is defined by the label of "made in India" on the package.

isoniazid and rifampicin are first-line antibiotics for tuberculosis (TB) mycobacteria. Because drug availability varies across purchase countries (in part because the targeted disease varies), we have 691 ciprofloxacin from all 18 purchase countries, 286 erythromycin from 11 countries, 223 isoniazid from 10 countries and 270 rifampicin from 11 countries. Our sample size on ciprofloxacin is greater than for other drugs in part because the initial rounds of data collection were more focused on ciprofloxacin and partly because there is more restricted access to TB medications. Further, some products were not available in markets where we expected them to be.

Out of the total 1470 "made-in-India" samples, 956 were bought within India, 430 bought from Africa, and 84 bought from Non-African countries outside of India (including China, Brazil, Russia, Turkey, Thailand) -- groups that we term Indian domestic, Africa, and Non-Africa purchases, respectively. For ciprofloxacin, we have data from all three purchase groups. For the other three drugs, the comparison focuses on Africa versus India domestic. Our regression methodology uses manufacturer-drug fixed effects to ensure that our comparison of drug quality within a manufacturer is also within the same drug type. With these controls, the difference between Africa and India domestic is identified in all drug types, while the difference between non-Africa and India-domestic is identified in ciprofloxacin only. While our main results are based on the full sample, later we will provide robustness checks on the subsample of ciprofloxacin only.

Table 1 summarizes drug quality and price by drug type and purchase country group. Prices are converted to US dollars by the exchange rate at the time of purchase and deflated to 2010 dollars. As detailed above, quality is measured by conformity to active pharmaceutical ingredient (API) content in a chromatographic assay. We define a sample as failing the basic quality test if its API is below 80% of the correct amount (per the label and benchmark authentic sample), with 0% API deemed falsified. Out of the 1470 samples, 10.9% failed basic quality tests, 103 (7%) were substandard and 57 (3.9%) were falsified.

Both antibiotics and TB drugs had more substandard than falsified products, which is consistent with mistake or negligence being more widespread than outright crime. As shown in Table 1, India domestic drugs are substantially cheaper than drugs purchased out of India, consistent with the literature (Cameron et al. 2008). However, drugs purchased from Africa are more likely to fail the TLC test than the same type of drugs in the Indian domestic group. In

comparison, drugs from Non-Africa have a greater passing rate than the Indian domestic ones for ciprofloxacin.

Many studies have shown that product registration is arguably the most important factor in ensuring drug quality in developing countries, although its practice varies greatly across countries (Bate et al 2010, Torstensson and Pugatch 2010). Our previous studies also show that registered and unregistered products differ significantly in both price and quality (Bate, Mathur and Jin 2011, 2014). In light of this, Table 2 groups the data by purchase country group and product registration status. Consistent with previous findings, registered products charge a higher price and are more likely to pass the TLC test.

Conditional on failing the TLC test, we find that registered products are more likely to be falsified than to be substandard, which is consistent with legitimate manufacturers following regulatory guidelines. The correlation between product registration status and purchase country group is interesting. Among registered products, we observe more falsified drugs than substandard drugs out of India, for both Africa and Non-Africa. Inside India, the percent of substandard drugs is slightly higher (3.3%) than falsified drugs (2.5%). Overall, the passing rates of registered products are similar across the three purchase groups, ranging from 91.9% to 94.4%. However, among non-registered products, the composition of passing, falsified and substandard drugs is vastly different across country groups. The passing rate in Africa is even below 50% -- worse than random chance – and the majority of failures are driven by substandard drugs. The passing rate inside India is also low (67.8%), with substantially more substandard drugs (22.6%) than falsified drugs (9.6%). Non-African countries are the best (100% pass), but the number of observations is very small. To summarize, these patterns suggest that the quality difference by purchase country group is mostly driven by non-registered products and substandard drugs account for the majority of problems in non-registered products.

In addition to product registration, several studies have demonstrated the role of the WHO prequalification[13] and retail chain status in drug quality (Bate, Jin and Mathur 2014; Bennett and Yin 2014). Of the 1,470 samples in our data, 80 are prequalified by the WHO and all of them appear to be registered. All but one of them passed our basic quality test; the one that failed has zero API and is probably a counterfeit. 42.65% of our sample were purchased from a

[13] http://www.who.int/topics/prequalification/en/

chain store[14] and 76.19% from a store that our covert shoppers subjectively assessed to be clean and tidy and professionally run. Consistent with the literature, purchases from chain store or more professional looking stores are more likely to pass our basic quality test. Table 2 further presents the breakdown of WHO prequalification, chain store purchases, and good-looking store purchases by product registration and purchase country groups. Not surprisingly, the percentage of WHO prequalified products and the percentage of products from chains or good-looking stores are all lower in African countries than in India Domestic or non-Africa.

Could these patterns be driven by Indian manufacturers or their export intermediaries exporting products of different quality to different countries? Table 3 regresses the dummy of passing the quality test on drug purchase country groups, with and without manufacturer-drug fixed effects (drug type fixed effects are included in the regression without manufacturer-drug fixed effects). We use linear probability model instead of probit in order to facilitate comparison with and without a large number of manufacturer-drug fixed effects.[15] The error terms are clustered by drug and purchase country group. Using the full sample, the first column finds significantly lower quality in Africa than in India domestic, while Non-Africa is statistically better than India domestic. This negative coefficient on Africa is even more conspicuous after we control for manufacturer-drug fixed effects in Column 2. With the fixed effects, Non-Africa and India domestic become statistically similar to each other. In the third and fourth columns, we redo the regressions for registered drugs only and find no significant difference across the three country groups. When we focus on non-registered drugs only, quality in Africa is significantly worse than Indian domestic, and quality in Non-Africa is the best. Again this pattern becomes even stronger in magnitude when we control for manufacturer-drug fixed effects, suggesting that they are driven by variations within the manufacturer-drug combination.

Table 4 presents two robustness checks for different subsamples. In the first three columns, we rerun Table 3 excluding the eight known counterfeits from China. The three columns are for all observations, registered drugs, and non-registered drugs respectively.

[14] A pharmacy was considered to be part of a chain if at least two distinct stores with similar layout and under the same retail logo were found in at least two different parts of the same city or multiple cities.

[15] Some of the 30 manufacturer-drug combinations have less than 10 observations in the cell, and these small cells may generate incidental parameter problem in probit with fixed effects. That being said, results are robust if we use probit instead of linear probability model (with the manufacturer-drug fixed effects). The probit results are available upon request.

Columns (4) to (6) repeat the exercise but focus on ciprofloxacin only. Every column controls for manufacturer-drug fixed effects. Both robustness checks display similar findings as in Table 3: drugs from Africa are more likely to fail than those from India or non-Africa and the failures are driven by non-registered products.[16]

IV. Further Data Analysis and Potential Interpretations

So far, we have discovered two interesting patterns regarding drug quality: first, "made in India" drugs purchased from Africa are of worse quality than those purchased within India, and from Non-Africa countries outside of India. This pattern is robust to manufacturer-drug fixed effects. Second, the above pattern is mostly driven by non-registered substandard products.

This section attempts to use data analysis and economic logic to explain these data patterns.

IV.1 Why do we observe the worst drug quality in Africa?

To highlight the differences between Africa, India domestic and Non-Africa, we collected country/city specific data in six dimensions: GDP per capita, adult literacy, the presence of any price control, maximum penalty for counterfeiting, Rule of Law (ROL) index, and International Property Right Index (IPRI).

In particular, the year- and city-specific GDP per capita data (adjusted for PPP) were constructed for 2009, 2010 and 2012 using city GDP estimates from PricewaterhouseCoopers (PWC 2009) and city population estimates from the 2009 revision of the UN's World Urbanization Prospects Report (UK 2009; UN 2009). The PWC city GDP estimates for 2008 were extended to 2009-2012 using country level GDP growth rates from the International Monetary Fund (IMF 2009-2012). City population estimates were extended forward to 2012 using the UN report's 2005–2010 average population growth and its 2015 estimated population growth figures (UN revisions for 2005-2010). For Accra, Kampala, Kigali, Lubumbashi, Lusaka and Maputo, city-level data were not available in some years, so we used country-level GDP per capita data from the IMF World Economic Outlook Database as of July 2014 (IMF 2014).

[16] In an unreported table, we further restrict the sample to ciprofloxacin only and exclude the eight known counterfeits from China. Results are very similar.

Male and female adult literacy rates were obtained from country-specific UNESCO data from 2009 and 2012, compiled from censuses and surveys conducted between 1999 and 2012. For four countries (Brazil, Egypt, Ethiopia and South Africa) UNESCO did not have 2009 figures. In these cases, we relied on the 2009 UNDP Human Development Report (UNDP 2009), which compiles country-specific data from censuses and surveys conducted between 1999 and 2007, which are also compiled by UNESCO (UN 2009). The literacy rates of these four countries are therefore slightly older than the rest. We take the average of female and male literacy rates as they are highly correlated (correlation coefficient = 0.89).

Price regulations include whether a purchase country issues price ceilings, mandatory retail prices, and/or price guidance. We hand-collected these regulations from each country's most recent government documents. Given the wide variety of price regulations across countries, a binary variable was defined as equal to one if a country has adopted any price regulation on pharmaceuticals in the data collection year and zero otherwise. For two observations, we use the closest later-year data to impute missing values in 2009.

We proxy ex post penalty for counterfeiters by the number of months a person will be sentenced to prison if he is found guilty for counterfeiting drugs. Minimum and maximum penalty were hand collected from the latest legal documents we could find in each country. To accommodate diverse sentencing guidelines, monetary fines are coded as zero months and the death penalty is coded as 360 months (30 years). We use maximum penalty in the analysis. For six countries, we could not find any information on maximum penalty, which accounts for 8.3% of the analysis sample.

Rule of Law index was constructed by the World Justice Project. Based on 100,000 household and expert surveys in 99 countries and jurisdictions, this index describes a nation's rule of law status by summarizing 47 indicators along nine themes: constraints on government powers; absence of corruption; open government; fundamental rights; order and security; regulatory enforcement; civil justice; criminal justice; and informal justice (WJP 2014). ROL index was first available in 2010, and has increased its country coverage from 66 countries in 2010 to 99 countries in 2014. If a country was covered by the ROL index since 2010, we use its 2010 ROL index for the data collection years before 2010 and its 2012 ROL index for the sample year of 2012. If a country was first covered by the ROL index in 2012 or 2014, we use the closest later-year ROL index to impute its missing value in earlier years. Of the 1470

observations, 10.9% have imputed ROL index, another 3.1% have missing values in the ROL index as ROL never covered 3 countries in our sample.

The IPRI index was constructed by the Property Rights Alliance (PRA), with the help of 74 international organizations and the Hernando de Soto Fellowship Program (PRA 2013). It measures the intellectual and physical property rights of 131 nations. The IPRI index was first available in 2007 and updated yearly since then. We use the IPRI index corresponding to the data collection year. If a country has missing values in a specific year, we use its closest later-year IPRI index to impute the missing value (2.1% of observations have imputed IPRI index).

Both ROL and IPRI indices provide a large number of indicators by detailed categories. Because these indicators are highly correlated, we use the overall ROL and IPRI indices. Countries that have missing values in the ROL index or maximum legal penalty carry a dummy variable indicating the missing data for the specific variable.

Table 5 summarizes the country/city specific characteristics in our sample. Table 6 shows their correlations. As expected, GDP per capita is positively correlated with adult literacy, rule of law, and IPRI index. Richer countries are more likely to have any price regulation, but the correlation between GDP per capita and maximum penalty for counterfeiting is much weaker.

In Table 7 Column 1, we repeat the basic regression from Table 3 Column 2 (dependent variable is whether a drug sample passes the TLC test). In Table 7 Column 2 we add product registration status, WHO prequalification, and what type of store the product was purchased from.[17] Alternatively, on top of Column 1, we include the six country/city characteristics to detect their influence on drug quality in Column 3. The last column of Table 7 includes all product and country/city characteristics. Manufacturer-drug fixed effects are always included.

As we expect, whether a product is registered and whether the product was purchased from a chain or professional-looking store are significantly correlated with passing the basic quality test, whenever they are included. However, the coefficient of WHO prequalification is always insignificant, likely because all WHO prequalified products are registered and we have included product registration in the same regression. More importantly, even after controlling for

[17] Note that we exclude price from this regression since price is very correlated with purchase country (given the large differences in income levels). Hence the price coefficient likely will pick up cross-country differences rather than the signaling effect of price within a country or country group. Also, price and quality are jointly determined by suppliers in response to local demand, thus including price on the right hand side will mask the effect of the other more fundamental differences across purchase country groups.

these product characteristics in Column 2, there is still a significant quality difference between Africa, India domestic and non-Africa, suggesting that product registration, WHO prequalification and retail store type are not enough to explain away all the quality difference by purchase country.

As shown in Column 3, when the regression only includes country/city attributes on the right hand side, both GDP per capita and having any price regulation have a significant coefficient. While we have expected higher income countries to have better drug quality, the negative coefficient on price regulation is a surprise. One possible explanation is that price ceiling may reduce the room to use price as a signal for quality. When we include both product attributes and country/city attributes in Column 4, the coefficient of GDP per capital remains positive (with marginal significance) but the coefficient of price regulation becomes insignificant. In both Columns 3 and 4, the coefficient of Africa is much closer to zero in magnitude and no longer significant.

Overall, these results suggest that, among all six country/city attributes, GDP per capita has the biggest statistical power explaining the quality differences across purchase country groups. In the mean time, product attributes including registration status, always play an important role in explaining drug quality.

IV.2 Which part of the supply chain is likely responsible for poor drug quality in Africa?

While income, local regulation, and retail network may all contribute to worse drug quality in Africa, the fight against poor drug quality requires more knowledge about the source of poor drug quality. Is it because Indian manufacturers cut corners or selectively export their inferior batches to Africa, or do some criminal counterfeiters pretend to be legitimate manufacturers? Maybe distributors also do a poor storage job along the supply chain which affects drug quality? Answering these questions will help improve drug quality, but direct evidence is extremely hard to get.

Even if the manufacturer label is correct, the manufacturer may prefer to claim a poor quality sample counterfeit and therefore circumvent its responsibility. Proof of criminal intent is, of course, a forensic question with many factors, not just product quality. We therefore do the best we can, and try to use economic logic to infer the most likely party responsible for poor-

quality drugs. Readers should note that our negative inferences, while based on the best available information and transparent assumptions, are not formal criminal accusations.

There are several possibilities regarding the true responsible party behind poor-quality drugs. In the first possibility, all manufacturer labels are correct but some Indian manufacturers or their export intermediaries intentionally export inferior products to Africa. This could happen because African countries are typically poorer, have a less educated population, and do not function well in regulating drug quality (Seiter 2010). In addition, facing more limits in economic resources, households in African countries may have a lower willingness to pay for a given increase in drug quality, even if they know the quality difference perfectly. This will create an economic incentive for manufacturers (or their export intermediaries) to either supply lower-quality products to a low-end market or exercise less quality control in such a market. We group all the above possibilities as intentional quality differentiation by purchase region. The second possibility is that counterfeiters (wherever they are based), who pretend to be the labeled Indian manufacturer, produce poorer-quality drugs in Africa because the risk of being caught is lower in African countries. Thirdly, wholesale distributors obtain the same quality of drugs from India, but they do a worse job in storing and distributing them within Africa. This could happen either because the cost of proper storage is too high in Africa or because distributors cut corners intentionally.

While poor distribution undoubtedly occurs in some settings (Bate 2012), for these drugs, which are not especially chemically labile, it is virtually impossible to reduce API from 100% to 0%. Hence, poor distribution cannot explain falsified products. Moreover, our previous paper analyzed a larger dataset of ciprofloxacin samples including those approved by stringent regulatory authorities (SRA) such as US Food & Drug Administration (Bate, Jin and Mathur 2014). In that paper, we found that SRA-approved ciprofloxacin, if containing any correct API, always passed the basic quality test regardless whether they were purchased from Africa or elsewhere.[18] This suggests that degradation should not be the main factor driving poor drug quality in Africa.

To check statistically whether poor storage and degradation may explain our findings, we collected each city's average daily high temperature per calendar month from weather-and-

[18] As reported in Bate, Jin and Mathur (2014), there are 89 SRA approved ciprofloxacin in our data: 88 of them passed the basic quality test and one was found to be falsified.

climate.com and worldweatheronline.com.[19] The four drug types in our sample, all in solid oral form (tablet or capsule), require storage at room temperatures no higher than 25°C or 30°C.[20] Therefore, from the weather data, we count the number of calendar months during which a city has an average daily high temperature above 30°C, and the number of months between 25°C and 30°C. Both counts are controlled for in the last three columns of Table 4, which repeats the Table 3 regressions with manufacturer-drug fixed effects. These results show that the coefficient of Africa is still negative after we add the temperature variables, although its statistical significance reduces slightly from 99% to 95% for the full sample regression and from 95% to 90% for the subsample of registered drugs or non-registered drugs.

In most cases, the coefficients for the two temperature variables are insignificant from zero. The only exception is the positive coefficient of months over 30°C in Column (7), which is against the predication that hotter cities are more likely to have quality problem due to poor storage condition. This is consistent with the raw correlation between weather and quality measures: the number of months in a year that have an average high temperature above 30°C is higher in India (9.44) than in Africa (3.14) or non-Africa (4.43), which is therefore unlikely to explain why the average drug quality is found higher in India than in Africa. For this reason, below we focus on the potential identity of manufacturer. It is still possible that although temperatures may be lower in Africa than India, that storage types (non-climate controlled metal structures that suffer from high temperatures) are worse in Africa. But we have no evidence for this. For all of the above reasons, below we focus on the potential identity of manufacturer.

To obtain an intelligent guess of whether the true manufacturer is the labeled Indian firm or a counterfeiter, we need a few more assumptions. In particular, we assume individual consumers cannot discern drug quality at the time of purchase, although there is some chance that sophisticated consumers or third-parties (e.g. government, NGOs, researchers) may discover poor quality drugs in the future.[21] This implies that today's market demand (q) only depends on

[19] Neither website covers all of our 22 cities. We obtain temperature data of 14 cities from weather-and-climate.com and the data of the other 8 cities from worldweatheronline.com.

20 We consulted fda.gov for the storage requirement of ciprofloxacin, healthcentral.com for isoniazid, drugs.com for erythromycin and webmd.com for rifampicin. Erythromycin is required to be stored in a tight container no higher than 25°C, the other three no higher than 30°C.

[21] It should be noted that arguably the most sophisticated NGO in the health sphere, Doctors Without Borders, was itself a victim of buying falsified HIV medications. So while NGOs may discover a problem, it is invariably after the fact.

observable manufacturer characteristics but it is more valuable to continue the business beyond today if the quality of today's product is good. For simplicity, let us assume drug quality can be good (G, with >80% API), substandard (S, with > 0% and < 80% API), or bad (B, with 0% API), and denote the value of continuing the business after today as V.

Now consider three types of "Indian" manufacturers that produce drug X in purchase country A: the first type is a real Indian firm that has registered with the government of A (referred to as "registered firm"); the second type is a real Indian firm that has not registered in A (referred to as "unregistered firm"); and the third type is a counterfeiter who may choose to pretend to be the registered firm or the unregistered firm. Consumers observe the labeled manufacturer identity and its registration status. All three types of manufacturers may choose to produce good (G), substandard (S), or bad (B).

For a registered firm, producing G today implies earning a normal profit margin today ($(p_r - c_G) \cdot q_r$) and keeping a good continuation value (V_r) for the future. If the discount rate is δ, the gain from good quality is $\pi_{r,G} = (p_r - c_G) \cdot q_r + \delta \cdot V_{r,G}$. In comparison, producing S or B means a higher profit margin today but a lower continuation value in the future. That is, $\pi_{r,S} = (p_r - c_S) \cdot q_r + \delta \cdot V_{r,S}$ and $\pi_{r,B} = (p_r - c_B) \cdot q_r + \delta \cdot V_{r,B}$, where $V_{r,G} > V_{r,S} > V_{r,B}$. Apparently, a registered firm prefers to produce good quality if the short run cost savings are smaller than the long run loss in continuation value.

$$\pi_{r,G} > \pi_{r,S} \text{ if } \delta \cdot (V_{rG} - V_{rS}) > (c_G - c_S) \cdot q_r;$$

$$\pi_{r,G} > \pi_{r,B} \text{ if } \delta \cdot (V_{rG} - V_{rB}) > (c_G - c_B) \cdot q_r.$$

Similarly, for an unregistered firm facing the same cost structure, we have

$$\pi_{nr,G} > \pi_{nr,S} \text{ if } \delta \cdot (V_{nr,G} - V_{nr,S}) > (c_G - c_B) \cdot q_{nr};$$

$$\pi_{nr,G} > \pi_{nr,B} \text{ if } \delta \cdot (V_{nr,G} - V_{nr,B}) > (c_G - c_B) \cdot q_{nr}.$$

Because product registration is costly, registered products often enjoy better price on the market and selling unregistered products is technically illegal, we believe the long run loss of producing poor quality is greater for registered firms. In other words, under the assumption that $\frac{(V_{rG} - V_{rS})}{q_r} > \frac{(V_{nr,G} - V_{nr,S})}{q_{nr}}$ and $\frac{(V_{rG} - V_{rB})}{q_r} > \frac{(V_{nr,G} - V_{nr,B})}{q_{nr}}$, registered firms should have more incentives to produce good quality products than unregistered firms.

The incentives of the counterfeiter are somewhat different. Because most counterfeiters are fly-by-night, we assume they only care about profit in the near future net of the potential risk

of being caught for counterfeiting. Since the penalty for counterfeiting is usually independent of whether the counterfeits contain any API, this implies that producing zero-API drugs always generates higher profits than producing drugs with correct API, regardless whom the counterfeiter pretends.

If counterfeiters will only produce bad quality drugs, the question is whether they should counterfeit registered products or unregistered products. Recall that registered products imply higher prices and a larger demand. Let F be the penalty of counterfeiting if caught. Assuming the chance of being caught is ρ_r for counterfeiting a registered product and ρ_{nr} for counterfeiting an unregistered product, the counterfeiter would prefer to pretend to be a registered firm if $(1-\rho_r)\cdot(p_r - c_B)\cdot q_r - \rho_r \cdot \mathrm{F} > (1-\rho_{nr})\cdot(p_{nr} - c_B)\cdot q_{nr} - \rho_{nr}\cdot \mathrm{F}$. In other words, the main tradeoff for the counterfeiter is the higher profit of counterfeiting registered products versus the potentially higher risk of being caught if he counterfeits registered products. If the chance of being caught is the same for counterfeiting registered and unregistered products, the counterfeiter will prefer to counterfeit registered products.

Above all, we argue that the counterfeiter most likely counterfeits registered products and produces the worst quality drug, as long as the drug quality is not observable to consumers, the penalty for counterfeiting is independent of drug quality, and the chance of being caught counterfeiting is about the same regardless of who the counterfeiter pretends to be. These arguments are supported by the eight cases of ciprofloxacin that were confirmed to be counterfeit from China by extra information from cooperate/government officers. All these eight counterfeits turned out to contain zero correct API and seven of them pretended to be a registered product. Conversely, the same logic implies that the substandard drugs in our data are unlikely driven by counterfeiters. If they are not driven by counterfeiters, they should be more likely driven by unregistered Indian firms than by registered Indian firms, because we know from the above paragraph that registered firms have already paid the cost of product registration and therefore should have more incentives to produce good quality drugs than non-registered firms.

Following this logic, we expand our data analysis by product registration status and detailed quality categories. In the first two columns of Table 8, we first repeat the basic quality regression (as in Column 2 Table 3, dependent variable = passing the basic quality test) and then add in the dummy of product registration as well as its interaction with the Africa and Non-Africa dummies. Manufacturer-drug fixed effects are always included. As we expect, registered

products are more likely to pass the TLC test. The coefficient of Africa*product registration is of similar absolute magnitude but opposite sign to the coefficient of the Africa dummy. This suggests that drug samples purchased in Africa are similar in basic quality from India domestic, if the samples are registered in the purchase country. Similar results apply to Non-Africa countries. In contrast, unregistered products still show significant quality difference between Africa (worst), India domestic, and Non-Africa countries (best).

In the next four columns of Table 8, we repeat these regressions but redefine the dependent variable as whether the drug sample is falsified, or whether the drug sample is substandard. The last two columns of Table 8 switch the dependent variable back to whether a drug sample passes the basic quality test, but restrict the sample to non-falsified samples only. Consistent with Table 2, these columns suggest that the biggest quality difference across purchase country groups concentrate in non-registered substandard products. According to the logic above, we believe the most likely explanation is that the labeled Indian manufacturers have produced the substandard products and they are not registered in the African destination. These results are robust to adding temperature variables or excluding the eight known counterfeit cases of ciprofloxacin.

V. Discussion

Overall, our sample of "Indian-made" medicines reveals two data patterns: first, drug quality is inferior among drugs purchased inside African countries compared to those purchased inside India or middle-income countries elsewhere. Second, unregistered substandard drugs containing insufficient API are the biggest driver of this quality difference in Africa. These findings are based on a low-tech API assessment of a limited number of drug samples, and had we used more advanced analytical methods, more failing drugs would have been detected. Therefore these are conservative conclusions.

Our sample frame is limited to a few anti-infective drugs, in a few countries, purchased from only storefront vendors, all of which restrict our ability to link the presence of substandard and falsified drugs to more detailed country-specific attributes. Furthermore, because our data were collected at the end of the distribution channel, it is difficult to separate the role of Indian manufacturers from those in the supply chain to retail pharmacies.

That being said, these findings provide suggestive, arguably worrisome evidence that some Indian drug companies and/or their export intermediaries segment the global medicine market into portions that are served by different quality medicines. While the notion of "export grade" marketing is familiar in other sectors such as agriculture, it appears to exist for medicines also, with Indian manufacturers and/or their export intermediaries likely exporting lower quality goods to Africa. One possible mechanism that may contribute to this result is quality differentiation by market demand. If consumers in poorer nations are more willing to accept less than perfect quality medicines in exchange for lower prices, Indian suppliers may simply be filling a market gap. Another possible driver is that African regulatory oversight is weaker (resulting in fewer registered products) as compared to middle-income countries elsewhere and Indians are more reluctant to sell the worst medicines in India itself, lest they be prosecuted.

There are alternative explanations, though none appear to be as likely. It is known that some organized criminals from China have counterfeited Indian products destined for Africa, although after this practice came to light and was denounced several years ago there appear not to be subsequent news reports of this crime recurring. Poor storage of initially good Indian products can also lead to degradation, although the environmental conditions favoring degradation (heat, light, humidity) are not worse, and apparently better, in Africa than India, where a lower rate of product failure was observed. Neither of these circumstances is the fault of Indian companies, but neither seems sufficient or likely to explain the data observations either. Africans are aware of their vulnerability to substandard and falsified medicines. At the time of this writing, West Africa and East Africa are trying to harmonize and improve their drug regulation practices.[22] Individual countries such as Nigeria and Ghana have banned sales from some Indian companies, and have pressured the Indian drug regulator. On one occasion, India's minister of state for commerce and industry even visited Nigeria and divulged the names of Indian companies producing fake medicines to boycott (Raufu 2003; Akunyili 2005). Since India's government feels that approach is necessary, regional, rather than simply national, regulatory action in Africa and blacklisting of transgressing Indian manufacturers might drive better performance from all Indian exporters.

There is also scope for collective security approaches. For example, in the civil aviation industry, regulators aim enforcement actions not against any single foreign airline that breaches

[22] Personal Communication with Andreas Seiter of the World Bank, March 12th 2014.

safety standards, but collectively target all the airlines of any foreign country that fails to uphold certain minimum standards. Under this collective regulatory response, in 2014 all Indian airlines were downgraded and lost the right to expand their flight operations in the United States—a development that gave India's aviation regulator powerful and urgent incentive to raise safety standards (the US restored their access in 2015).[23] Applying this approach to medicines, if drug regulators from Africa, America and Europe jointly decided to impose tougher quality inspection practices on Indian-sourced products as a whole, it very likely would eliminate all incentive for Indian manufacturers or their export intermediaries to export failing medicines.

A softer response to these findings would be simply to increase informational flows to African doctors and pharmacists about the possible inferior quality of some Indian drugs; even just naming Indian companies repeatedly found to sell substandard medicines. While many African doctors anecdotally are already wary of Indian medicines, such an effort might further drive the African middle classes away from many Indian products.

Lastly, although this paper has focused on Indian produced medicines, India is by no means the only large exporter of drugs. It is not our intent to single out any one manufacturing country as being solely or largely responsible for the quality problem. Our data so far has only allowed us to work on products that are labeled "made in India" and prohibited us from statistical comparison across manufacturing countries. Further research into the drug quality of Chinese and other manufacturing countries would be useful to understand how widespread the problem may be.

[23] http://www.thehindu.com/business/us-downgrade-to-hit-all-indian-airlines-capa/article5653620.ece

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Table 1 Summary of drug quality and price by drug type and purchase country

	India Domestic	Africa	Non-Africa	Total
ciprofloxacin				
N	456	151	84	691*
pass	91.9%	88.1%	95.2%	91.5%
falsified	4.8%	3.3%	4.8%	4.5%
substandard	3.3%	8.6%	0.0%	4.1%
price	1.552	5.745	11.229	3.645
Erythromycin				
N	167	119	0	286
pass	87.4%	80.7%	.	84.6%
falsified	1.8%	7.6%	.	4.2%
substandard	10.8%	11.8%	.	11.2%
price	0.749	3.780	.	2.010
Isoniazid				
N	166	57	0	223
pass	93.4%	84.2%	.	91.0%
falsified	1.8%	8.8%	.	3.6%
substandard	4.8%	7.0%	.	5.4%
price	1.542	4.122	.	2.202
Rifampicin				
N	167	103	0	270
pass	89.8%	80.6%	.	86.3%
falsified	2.4%	1.9%	.	2.2%
substandard	7.8%	17.5%	.	11.5%
price	1.466	4.227	.	2.519
Total				
N	956	430	84	1470
pass	91.0%	83.7%	95.2%	89.1%
falsified	3.3%	4.9%	4.8%	3.9%
substandard	5.6%	11.4%	0.0%	7.0%
price	1.395	4.622	11.229	2.901

Note: A drug is labeled "pass" if the active pharmaceutical ingredients (API) of the test sample is at least 80% of the required API, labeled "falsified" if no API can be detected in the test sample, labeled "substandard" if the detected API is strictly above 0% but below 80%. Price is converted to 2010 US$. * As noted in the paper, 8 ciprofloxacin samples were confirmed to be counterfeits from China by extra information from cooperate/government officers. We keep them in the sample because they are labeled "Made in India" on the package.

Table 2 Summary of drug quality and price by registration status and purchase country

	India Domestic	Africa	Non-Africa	Total
Non-registered				
N	115	83	12	210
pass	67.8%	49.4%	100.0%	62.4%
falsified	9.6%	6.0%	0.0%	7.6%
substandard	22.6%	44.6%	0.0%	30.0%
WHO prequalified	0	0	0	0
Purchased in a chain store	0	18.07%	0	7.14%
Purchased in a good-looking store	49.57%	34.94%	100%	46.67%
price	1.148	3.788	8.397	2.605
Registered				
N	841	347	72	1260
pass	94.2%	91.9%	94.4%	93.6%
falsified	2.5%	4.6%	5.6%	3.3%
substandard	3.3%	3.5%	0.0%	3.2%
WHO prequalified	5.94%	5.76%	13.89%	6.35%
Purchased in a chain store	47.09%	49.86%	59.72%	48.57%
Purchased in a good-looking store	84.30%	70.03%	97.22%	81.11%
price	1.429	4.822	11.702	2.950
Total				
N	956	430	84	1470
pass	91.0%	83.7%	95.2%	89.1%
falsified	3.3%	4.9%	4.8%	3.9%
substandard	5.6%	11.4%	0.0%	7.0%
WHO prequalified	5.23%	4.65%	11.90%	5.44%
Purchased in a chain store	41.42%	43.72%	51.19%	42.65%
Purchased in a good-looking store	80.13%	63.26%	97.62%	76.19%
price	1.395	4.622	11.229	2.901

Note: A drug is labeled “pass” if the active pharmaceutical ingredients (API) of the test sample is at least 80% of the required API, labeled “falsified” if no API can be detected in the test sample, labeled “substandard” if the detected API is strictly above 0% but below 80%. Price is converted to 2010 US$.

Table 3 Basic quality regressions

Sample	Full		Registered only		Non-registered only	
Dependent Variable	Pass	Pass	Pass	Pass	Pass	Pass
	(1)	(2)	(3)	(4)	(5)	(6)
Africa	-0.0650***	-0.0847***	-0.0189	-0.0258	-0.147***	-0.185***
	(0.0106)	(0.0174)	(0.0114)	(0.0142)	(0.0341)	(0.0552)
Non-africa	0.0268***	0.0123	0.00104	-0.0118	0.193***	0.272***
	(0.007)	(0.0090)	(0.0075)	(0.0066)	(0.0123)	(0.0531)
Erythromycin	-0.0524***	absorbed	-0.0327**	absorbed	-0.253***	absorbed
	(0.0084)		(0.0123)		(0.058)	
Isoniazid	0.00137	absorbed	0.0166	absorbed	-0.267**	absorbed
	(0.0107)		(0.0111)		(0.0948)	
Rifampicin	-0.0378**	absorbed	0.00681	absorbed	-0.331***	absorbed
	(0.0126)		(0.0092)		(0.00655)	
Constant	0.926***	0.915***	0.943***	0.943***	0.807***	0.682***
	(0.007)	(0.0059)	(0.0075)	(0.0049)	(0.0123)	(0.022)
Manufacturer-drug FE	No	Yes	No	Yes	No	Yes
Observations	1,470	1,470	1,260	1,260	210	210
R-squared	0.018	0.119	0.006	0.090	0.154	0.315

Note: Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Default group is India domestic, ciprofloxacin. All regressions use linear probability model. Errors are clustered by drug-countrygroup where countrygroup is defined Africa, Nonafrica and India domestic.

Table 4 Robustness checks for basic quality regressions

	Excluding 8 known counterfeits			Ciprofloxaxin only			Full Sample With Temperature Data		
Sample	All	Registered only	Non-registered only	All	Registered only	Non-registered only	All	Registered only	Non-registered only
Dependent Variable	quality	quality	quality	quality	quality	quality	quality	quality	quality
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Africa	-0.0807***	-0.0236	-0.180**	-0.0435**	0.0110**	-0.101*	-0.0653**	-0.0354*	-0.244*
	(0.0196)	(0.0155)	(0.0559)	(0.00590)	(0.00217)	(0.0309)	(0.0213)	(0.0155)	(0.113)
Non-Africa	0.00786	-0.0155*	0.264***	0.0243**	-0.00214	0.319***	0.0306**	-0.0183	0.212
	(0.0115)	(0.00809)	(0.0559)	(0.00512)	(0.00437)	(0.0263)	(0.0126)	(0.0146)	(0.118)
# of calendar months in a year with average daily high temperature at or above 30°C							0.00416**	-0.00122	-0.00916
							(0.00138)	(0.00275)	(0.0125)
# of calendar months in a year with average daily high temperature between 25°C and 30°C							0.00239	0.000790	-0.00450
							(0.00165)	(0.00294)	(0.0133)
Manufacturer-drug fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,462	1,253	209	691	581	110	1,470	1,260	210
R-squared	0.112	0.068	0.314	0.082	0.104	0.288	0.120	0.090	0.317

Note: Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Default group is India domestic, ciprofloxacin. All regressions use linear probability model. Errors are clustered by drug-countrygroup where countrygroup is defined Africa, Nonafrica and India domestic.

Table 5 Country characteristics

country	city GDP per capita	adult literacy rate (%)	have any price regulation	max legal penalty for counterfeiting (month in jail)	Rule of Law index	Intellectual Property Right Index (IPRI)
Angola	7082	71	1	60	N.A.	3.46
Brazil	20514	96.7	1	180	0.58	5.33
China	17196	95	1	360	0.48	5.50
DRC	197	65	0	N.A.	0.48	4.94
Egypt	14166	71.5	1	36	0.50	5.02
Ethiopia	4782	36.8	0	240	0.42	4.13
Ghana	1663	67.6	0	60	0.54	5.26
India	9110	64.7	1	360	0.50	5.47
Kenya	3516	82.4	0	60	0.37	4.36
Mozambique	1128	50.6	0	N.A.	N.A.	4.60
Nigeria	3386	58.1	0	360	0.42	3.80
Russia	31614	99.6	1	120	0.43	4.48
Rwanda	1305	66.9	1	N.A.	N.A.	5.92
Tanzania	2717	71.5	0	N.A.	0.49	4.71
Thailand	17789	98.4	0	240	0.54	5.22
Turkey	16945	94.1	1	N.A.	0.51	5.30
Uganda	1258	73.5	0	240	0.42	4.16
Zambia	1679	67.6	0	N.A.	0.46	4.57
Total	8261	67	0.76	304.3	0.49	5.19

Note: N.A. stands for “data not available.” In all countries except India, we cover only one city, GDP per capita is for that city in the sample year. In India, we cover five cities, GDP per capita of India is the average across the five cities.

Table 6 Correlation of country characteristics

	city GDP per capita	adult literacy rate (%)	have any price regulation	max legal penalty for counterfeiting (month in jail)	rule of law index	IPRI index
city GDP per capita	1					
adult literacy rate (%)	0.4341***	1				
have any price regulation	0.6018***	-0.0482*	1			
max legal penalty for counterfeiting (month in jail)	0.1160***	-0.3216***	0.5157***	1		
rule of law index	0.2037***	0.1478***	0.3679***	0.1131***	1	
IPRI index	0.3743***	0.0416	0.6488***	0.3944***	0.6562***	1

*** p<0.01, ** p<0.05, * p<0.1. Correlations are conditional on non-missing values.

Table 7 Why do African countries receive worse-quality drugs?

	pass	pass	pass	pass
	(1)	(2)	(3)	(4)
Africa	-0.0847***	-0.0373**	-0.0107	-0.00681
	(0.0174)	(0.0154)	(0.0735)	(0.0854)
Non-africa	0.0123	0.0243*	-0.0751	-0.106
	(0.00902)	(0.0106)	(0.0550)	(0.0644)
Product registered		0.275***		0.287***
		(0.0565)		(0.0573)
WHO prequalification		-0.00527		-0.00933
		(0.0171)		(0.0192)
Purchased from chain store		0.0682***		0.0707***
		(0.0130)		(0.0169)
Purchased from a store that the shopper		0.0909***		0.0873***
assessed good-looking		(0.0212)		(0.0233)
Max Legal Penalty			0.000272	0.000122
			(0.000158)	(0.000188)
Rule of Law Overall Index			0.180	0.140
			(0.271)	(0.198)
IPRI Overall Index			0.0291	0.00360
			(0.0353)	(0.0381)
City GDP per capita (in 1000)			0.0109***	0.00984*
			(0.00246)	(0.00499)
Adult Literacy Rate			-0.000310	0.000794
			(0.00116)	(0.00109)
Have any price regulation			-0.0564**	-0.0369
			(0.0192)	(0.0455)
Manufacturer-drug FE	yes	yes	yes	yes
Observations	1,470	1,470	1,470	1,470
R-squared	0.119	0.251	0.124	0.257

Notes: Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Default group is India domestic. All regressions use linear probability model. All regressions control for missing-value dummies for Rule of Law index and maximum legal penalty, as well as imputed-value and/or missing-value dummies for the Rule of Law index, IPRI index, maximum legal penalty, and price regulation. Errors are clustered by drug-countrygroup where countrygroup is defined Africa, Non-africa and India domestic.

Table 8 Regressions on purchase region and product registration status, by quality categories

Sample	Full		Full		Full		Non-falsified	
Dependent Variable	pass	pass	falsified	falsified	substandard	substandard	pass	pass
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Africa	-0.0847***	-0.161*	0.0250	-0.0355	0.0597***	0.196*	-0.0636***	-0.191*
	(0.0174)	(0.0778)	(0.0152)	(0.0341)	(0.0174)	(0.102)	(0.0173)	(0.0954)
Non-Africa	0.0123*	0.330***	0.0169**	-0.104***	-0.0292***	-0.226***	0.0318***	0.257***
	(0.009)	(0.0425)	(0.0073)	(0.030)	(0.0053)	(0.0565)	(0.0055)	(0.0552)
Product registered		0.290***		-0.0692***		-0.221**		0.249***
In purchase country		(0.0597)		(0.023)		(0.0716)		(0.0694)
Africa * product-registered		0.129		0.0669		-0.196		0.188
in purchase country		(0.0788)		(0.0415)		(0.133)		(0.105)
Non-Africa * product-registered		-0.351***		0.136***		0.214**		-0.241***
in purchase country		(0.0512)		(0.0257)		(0.0649)		(0.0624)
Manufacturer-drug FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,470	1,470	1,470	1,470	1,470	1,470	1,413	1,413
R-squared	0.119	0.237	0.155	0.163	0.098	0.245	0.101	0.259

Notes: Robust standard errors in parentheses. *** p<0.01, ** p<0.05, * p<0.1. Default group is India domestic. All regressions use linear probability model. Errors are clustered by drug-countrygroup where countrygroup is defined Africa, Nonafrica and India domestic.