Drug Registration - a necessary but not sufficient condition for good quality drugs – a preliminary analysis of 12 countries

Africa Fighting Malaria Working Paper

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Summary

As the United States has demonstrated over the past century, drug quality is partly dictated by the drug regulatory environment. Without at least basic quality control, cheats can flourish and quality can be weakened. This paper discusses the most basic of quality controls, the registration of drugs by a competent agency, in a variety of countries, and shows that there are many differences between countries known to have drug quality problems.

Introduction

There is a tacit assumption amongst healthcare workers that all drugs of the same therapeutic type, whether innovator brands, generic brands, or a variety of copies of the product, are interchangeable. While there may be concern that some countries' products are more likely to be counterfeited, if one assumes the product is genuine, then the assumption holds that the product will work.

But anecdotal reports suggest that, even when counterfeits and otherwise obviously degraded or grossly substandard products are identified and removed from any sample set, quality problems remain for some products. Given that western countries source so many drug ingredients from abroad, for instance, up to 80% of the active ingredients in U.S. drugs are now made overseas,[4] news reports of nefarious activity have made westerners wary of drugs produced in emerging economies. A recent Pew Trusts poll indicated that 54% and 70% of Americans distrusted drugs sourced respectively in India and China.[5] But it is not acceptable in international trade law to boycott products based on suspicion alone, nor is it prudent since many drugs made in emerging economies are demonstrably fine and are certainly cheaper than innovator brands.

This working paper is the first part of a project looking at various characteristics, including product variability, of essential drugs in developing and mid-income countries. The publication that will follow this paper will assess actual drug variability; this working paper addresses what is probably a significant driver of drug quality – the legislative environment, and in particular, the registration process in which medicines are made and, more critically, sold.

Background

The registration process is perhaps the most important as well as the simplest part of product regulation. In economic jargon, product registration is probably a necessary but not sufficient condition for good quality medicines. Obviously, such products can exist in a country that has not registered them, but these will probably have been brought in for personal use or perhaps smuggled.

The lack of drug registration is a serious and well-documented problem to varying degrees across all 12 countries examined in this paper.[6] By some estimates, as much as 30% of the drugs in

[4] "PEW Prescription Project Press Release," *PEW Prescription Project* (3 August 2010) Available at: http://www.prescriptionproject.org/news/pressreleases?id=0026 Accessed 9 September 2010
[5] Ibid.
[6] These are: Argentina; Brazil; China; India; Kenya; Nigeria; Peru; Russia; Thailand; Turkey; Uganda; Vietnam.

Brazil are not registered,[7] while in Nigeria 19% of drugs on the market were not registered as of 2006.[8] In Vietnam, a 2006 study on anti-malarial drugs discovered that 60% of anti-malarial samples were not registered.[9] In Kenya, a separate study in 2007 found that 42% of anti-malarials were not registered.[10] Unregistered pharmaceuticals can easily be found in informal markets, they can also be found in the formal health sector – hospitals, pharmacies, wholesalers and medicine stores. Some pharmacists sell them unknowingly, while others buy unregulated products from traders to save money. By and large, unless a competent authority oversees drugs entering a country, and where applicable those produced domestically, it is likely that product quality will be more varied.

Some of these medicines are produced in laboratories, which may or may not have a good manufacturing practice (GMP) license or be registered to produce that particular medicine; others are made in backyard shacks. In China, for instance, the State Food and Drug Administration (SFDA) reported that in 2007 there were 329,613 cases of unlicensed drugs, most of which were manufactured by 'fly by night' firms.[11] In Russia, legitimate drug companies are known to produce unregistered medicines on the side for extra profit; from 2002-2005, Russian officials estimated seizures of over 1,000 tons of illicitly manufactured pharmaceuticals.[12] Many unregistered products are also imported or smuggled, especially where regulatory presence and control along the borders are weak, such as in Thailand.

In Brazil and Argentina, registered medicines are still not necessarily bioequivalent to the originals they imitate; in these countries, there is a third, controversial class of drugs called 'similars,' which are not required to be bioequivalent to innovator brands.[13] Recognizing that similars constituted the majority of substandard medicines in the country, Brazil's regulatory agency, ANVISA, changed its legislation in March 2003, requiring that similar manufacturers submit bioavailability data, pharmaceutical equivalence tests, and a copy of an ANVISA-issued GMP certificate during registration.[14] Similar manufacturers registered before 2003, however, have until 2014 to comply. While this grace period is not ideal from a public health standpoint, it is a step in the right direction on behalf of Brazil; unlike Brazil, Argentina has not expressed any intent to require bioequivalence testing for similars in order to become registered.

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[7] "Brazil one of the top emerging markets for Pharma," *Thepharmaletter (16 March 2009) Available at:* http://www.thepharmaletter.com/file/13345/brazil-one-of-the-top-emerging-markets-for-pharma-with-current-growth-of-23-pa.html Accessed 8 September 2010

[8] "Transnational Trafficking and the Rule of Law in West Africa," *United Nations Office of Drugs and Crime* (July 2009) Available at: http://www.unodc.org/documents/data-and-analysis/Studies/West_Africa_Report_2009.pdf Accessed 17 September 2010

[9] Hall, K.A., Newton, P.N., Green, M.D., et al, "Characterization of counterfeit artesunate antimalarial tablets from Southeast Asia," *American Journal of Tropical Medicine and Hygiene* 2006: *75*(5) Available at: http://www.ajtmh.org/cgi/content/full/75/5/804 Accessed 17 September 2010

[10] "Anti-malarial Medicines in Kenya: Availability, Quality, and Registration Status," *WHO and HAI* (December 2007) Available at: http://apps.who.int/medicinedocs/documents/s16424e/s16424e.pdf Accessed 24 June 2010; p.8

[11] "Regulators struggle to tame fake medicine market" *China Daily* (25 May 2009) Available at: http://www.chinadaily.com.cn/bw/2009-05/25/content_7937588.htm Accessed 10 September 2010

[12] "Russia in new crackdown on counterfeits," *Daily International Pharma Alert* (27 December 2005) Available at: http://www.fdanews.com/newsletter/article?articleId=83366&issueId=8849 Accessed 16 September 2010

[13] "Registration of Medicines," *ANVISA Website* (2010) Available at: http://www.anvisa.gov.br/eng/drugs/registration.htm Accessed 8 September 2010

[14] "Resolution-RDC 133 of 20 May 2003," *ANVISA Website* (2010) Available at: http://www.anvisa.gov.br/eng/legis/resol/133_03_rdc_e.htm Accessed 10 September 2010

The U.S. Food and Drug Administration (FDA) was established in 1906 to combat “cheats” who sold adulterated products and could do so because prior to that there were no standards enforced uniformly. Of course product registration is not sufficient, not least because the authority could register products without conducting proper analysis, but it is generally necessary for a start.

One way for companies to cheat is to send well-made products as the samples for registration to pass tests, and then sell products produced under less stringent and less costly conditions. This is a key reason why the production processes of domestically made drugs, and not just the drugs themselves, need to be inspected before product registration is given. GMP certification is important, as is post-marketing surveillance, which is the random sampling of products on the market required in each country to ensure product quality is consistent. Adverse Drug Reaction (ADR) reporting is also important. Comparing the legislative environment as well as these other factors is far harder than the simple yes/no of whether a product is registered. So this investigation starts with product registration.

This paper assesses product registration practices in a selection of key countries, such as India, China, Brazil and many African nations. Most of these countries have, or will have, drug samples collected from them to be analyzed in later studies.

Results

Table 1 highlights the different registration procedures in the 12 countries analyzed. It is immediately clear that, while many of the application requirements are the same, the specifics about what companies have to do in order to get their products registered varies. Among other things, differences were observed in the costs of registration, quality analysis requirements, the length of evaluation processes, the duration of registration certificates, renewal policies, and GMP compliance. In general, the cost of registering a product varies from a few hundred dollars in countries like Uganda, to many thousands of dollars in places like Russia and Brazil. Often fees differ depending on whether the drug is locally produced or imported, and if it is a generic or innovator product.

Some countries require that significant amounts of clinical trial or bioequivalence data be submitted with registration applications, while other countries do not specify if any such data is required, and still others, like Brazil and Argentina, which allow ‘similars’, specifically require no bioequivalence data for their registration. Most of the countries under study require two or three drug samples be submitted with applications for analysis, but in Vietnam only about 10% of all applications include sample analysis.

Significant differences can also be seen in the length of time it takes various drug authorities to evaluate registration applications (See Figure 1). While the average evaluation period was between three to six months in developing countries and 12-18 months in emerging countries, in Peru, drug approvals are determined within just seven days. This is much faster than even the fast-track registration offered by some countries for priority drugs, which still takes at least one month. But Peru’s approach is flawed, because if a drug application has not been evaluated within seven days of its receipt, it becomes automatically registered, though under a law passed

by Peruvian Congress in 2009, it is expected that this timeline will be extended to six months.[15] Similarly, in Brazil, if ANVISA fails to accept or reject a registration application within 180 days of its receipt, that product will automatically become registered.[16,17]

In Thailand, because drugs are not required to go through renewal processes after achieving initial registration, many unsuitable or inappropriate drug formulas registered decades ago may still be on the market. For instance, according to the Thai FDA, 230 drug formulas registered in 1983 remain on the market today, having undergone no reviews in nearly 26 years.[18] On top of this, Thailand has also been slow to recall medicines with probable adverse effects; from 2002 to 2008, only 17 registered drugs were withdrawn in Thailand,[19] whereas in Nigeria at least 10 registered drug products were recalled from the market in 2009 alone.[20,21]

Similar variations exist between the countries' registration renewal policies. In most of these countries registration certificates are valid for five years, after which re-registration of a drug is required. In India, re-registration is required every three years, whereas in Thailand it is never required.[22] Furthermore, in Russia, if a drug is granted re-registration, it is granted an open-ended certificate, whereas in Nigeria, an imported drug can only be re-registered once (for an additional five years) before it has to start being produced locally. Many governments desire local production of drugs, preferably by country nationals to provide jobs and income, but Nigeria mandates it.

While some countries have regulatory authority websites detailing registration procedures, the quality and accessibility of these sites vary significantly, some being so obscure that registration is difficult and prolonged.[23] For instance, despite claims that registration for foreign manufacturers has been made simpler, Russia's (Rozdravnadzor) webpage is still only available in Russian, and it is suggested that companies hire an authorized agent to undertake registration. Unsurprisingly, it is estimated that registration for importing pharmaceuticals into Russia takes between 12 and 18 months.[24]

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[15] "Multisource drug policies in Latin America: survey of 10 countries," *World Health Organization* (January 2005) Available at: http://www.who.int/bulletin/volumes/83/1/en/64.pdf Accessed 2 July 2010

[16] "Drug Registration in Brazil," *PharmaBiz* (25 July 2005) Available at: http://www.pharmabiz.com/article/detnews.asp?articleid=28834&sectionid=50 Access 20 September 2010

[17] "Medical Device Regulatory Requirements for Brazil," (21 March 2002) Available at: http://www.ita.doc.gov/td/health/brazilregs.pdf Accessed 19 September 2010

[18] "Drug Registration Needs Overhaul" (2010) Bangkok Post Available at http://www.bangkokpost.com/news/investigation/31670/drug-registration-needs-overhaul Accessed 7 September 2010

[19] Ibid.

[20] "Pharmacovigilance- FDIC News," *NAFDAC* Vol 3 No. 1, 2009 Available at: http://www.nafdac.gov.ng/nafdac-newsletter Accessed 14 September 2010

[21] Ibid.

[22] "Drug Registration Needs Overhaul," Bangkok Post (24 January 2010) Available at: http://www.bangkokpost.com/news/investigation/31670/drug-registration-needs-overhaul Accessed 10 September 2010

[23] "Drug regulatory requirements in Russia," *Pharmabiz.com* (24 June 2004) Available at: http://www.pharmabiz.com/article/detnews.asp?articleid=22502&sectionid=50 Accessed 3 August 2010

[24] "Navigating Pharmaceutical Product Registration in the Russian Federation," *DRW Monthly* (November 2009) Available at: http://www.drw-research.com/newsletter/Nov%2009.htm Accessed 1 August 2010

Similar problems were found in accessing online registered drug lists intended to help local consumers. For instance, Brazil's (ANVISA) list of registered medicines, was 'under construction', and the link to Peru's (DIGEMID) registered drug list was broken. India's registered drug list online was organized by year of registration, with no cross-referenced index, with lists for each state, not the country as a whole. Finding any information on Vietnam was made more difficult since its site was only in Vietnamese. And although in China the registration process is in English, the list of approved drugs was only in Chinese. Thailand's registration website was relatively complete and easy to navigate, but also required translation. Kenya, Uganda and Nigeria had accessible, up-to-date, and navigable drug registration databases and web-pages.

Discussion

African nations have a greater level of transparency and organization, and this may be the direct result of demands made by donors that require such information to be readily available and accessible.

India is unusual in not having a central drug regulatory authority to control both drug product registration and manufacturing quality. Manufacturing, laboratory, and sales standards are controlled by individual states in India: Maharastra and Andra Pradesh have good reputations for enforcing GMP; others such Haryana and Uttar Pradesh do not live up to the same standards.[25] The Mashelkar Report (2003) found that of 31 states, only seven possessed properly equipped laboratories capable of fulfilling the functions of regulating manufacture and sales of medicines. This causes problems, as a drug licensed by the Central Drugs Standard Control Organization (CDSCO) and approved for manufacture in one state may be sold in other states without further interference, unless due cause can be shown that it may be harmful.[26] Furthermore, CDSCO is responsible for monitoring adverse drug reactions, but individual states are responsible for the recall procedure. Additionally, individual states inspect and approve manufacturing sites, but CDSCO is responsible for World Health Organization GMP certification.

For instance, in 2008, the regulatory authority of Maharastra state detected 547 samples of substandard drugs, of which 421 were manufactured in Himachal Pradesh, Karnataka and Andhra Pradesh.[27] Haryana has established a zero tolerance policy where producers of substandard medicines can be blacklisted, but there is little evidence this is working because neither Haryana nor CDSCO have any authority to enforce manufacturing standards on other states. Part of the general problem is that drug inspectors are severely understaffed and underpaid, and regrettably some have been caught taking bribes, often as little as $100, in order to overlook discrepancies.

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[25] "FDA review reveals sale of inferior drugs," *Times of India* (28 January 2009) Available at: http://timesofindia.indiatimes.com//city/mumbai/FDA-review-reveals-sale-of-inferior-drugs/articleshow/4039057.cms Accessed September 2010

[26] Pugatch, Dr. Meir and Dr. David Torstensson. "Keeping Medicines Safe," *Stockholm Network* (2010) p. 52 Available at: http://www.stockholmnetwork.org/downloads/publications/Keeping_Medicines_Safe_Final_Draft_2010.pdf Accessed June 15, 2010

[27] "FDA review reveals sale of inferior drugs," *Times of India* (28 January 2009) Available at: http://timesofindia.indiatimes.com//city/mumbai/FDA-review-reveals-sale-of-inferior-drugs/articleshow/4039057.cms Accessed September 2010

China has a central authority but de facto control of production is by the states; it too suffers from drug inspectors who have accepted bribes, some being punished severely, even given the death penalty.[28] Enforcement of the removal of dubious products from the market is uneven. Products which are not registered, or registered with fake GMP certificates, cause a considerable problem in the Chinese market. In June 2010, China's drug regulator banned the export of raw materials from 10 Chinese drug companies since they were supplying products without proper GMP certificates. These drugs were being exported to India, and as a result, the Drugs Controller General of India (DCGI) cancelled registration of approximately six Chinese companies, and a few other companies surrendered their own licenses because they did not comply with GMP.[29]

In Uganda, when high-ranking officials were found guilty of accepting bribes in exchange for registering substandard medicines, the National Drug Authority (NDA) reinstated the ministers in their positions within the Ministry of Health almost immediately after they posted bail.[30] Even worse, the whistle-blower, a subordinate, lost his job and in replacing him, an advertisement for the job was posted with specifications for qualifications that were lower than his.[31]

In other countries, corruption occurs more quietly, often among the members of the registration approval committees. In both Nigeria and Thailand, there is a lack of transparency regarding not only the members of these committees and their necessary qualifications, but also regarding their decision-making process for approvals.[32,33] In Russia and Uganda, similar problems exist in that affluent political figures have been directly tied to questionable quality local production ventures, abusing their power and influence behind the scenes for profit.[34,35,36]

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[28] Arana Eunjung Cha. "China executes former Head of Food, Drug Safety," *Washington Post* (11 July 2007) Available at: http://www.washingtonpost.com/wp-dyn/content/article/2007/07/10/AR2007071000165.html Accessed 8 September 2010

[29] "Drug regulator bans raw material import from 10 Chinese firms," (15 June 2010) Available at: http://economictimes.indiatimes.com/news/news-by-industry/healthcare/biotech/pharmaceuticals/Drug-regulator-bans-raw-material-import-from-10-Chinese-firms/articleshow/6048536.cms Accessed 22 June 2010

[30] Folusho De- grata Shado, "The Torn Veil: Access to information as a tool for combating corruption with reference to Uganda," *Sunday Vision* (10 October 2004)Available at: https://www.up.ac.za/dspace/bitstream/2263/1101/1/shado_fd_1.pdf Accessed 10 September 2010

[31] Ibid.

[32] "Measuring transparency in medicines registration, selection and procurement – Four country assessment studies" *World Health Organization* (2006) Available at: http://www.who.int/medicines/areas/policy/goodgovernance/Transparency4CountryStudy.pdf Accessed 17 September 2010

[33] Amundsen, Inge et al., "Corruption, lack of political will and the role of donors (in Uganda)," *Working Paper* (December 2005)Available at: http://www.sed.manchester.ac.uk/research/events/conferences/documents/Redesigning%20The%20State%20Papers/Amundsen.pdf Accessed 10 September 2010

[34] "Pharmaceuticals executives given suspended sentences for counterfeit medicines," *MosNews* (3 April 2009) Available at: http://www.mosnews.com/money/2009/04/03/751/ Accessed 13 July 2010

[35] "RosZdravNadZor chief slams justice system," *Russian Pharmaceutical Review: Volume 1 No.3* (March 2009). Available at: http://www.ssees.ucl.ac.uk/RPR.pdf Accessed 3 August 2010

[36] "Uganda Health Ministry diverts ARV money," *PlusNews* (10 August 2009) Available at: http://www.plusnews.org/Report.aspx?ReportId=85658 Accessed 10 September 2010

Conclusion

Tolstoy's Anna Karenina described happy families as all alike, but every unhappy family is unhappy in its own way. There can be no doubt that there is a decidedly unhappy situation for many people who buy substandard drugs, and the causes appear to vary in the countries in this paper. And although drug regulatory systems are not identical in developed nations, they do similar things, which most developing nations cannot do. Given the limited analysis presented in this paper, one would think the aim of poorer nations would be to try and cover as many of the activities undertaken by the developed nations' regulatory authorities, in order to lower incidences of substandard drugs on their own markets. Future studies will analyze the actual variability of drugs on these markets.

Table 1: Registration Procedures by Country

	Argentina	Brazil	China	India	Kenya	Nigeria[37]	Peru	Russia	Thailand	Turkey	Uganda	Vietnam
Authority responsible for registration	ANMAT	General Office of Medicine (GGMED) located in ANVISA	State Food and Drug Admin. (SFDA)	Drug Controller General of India (DCGI)	Committee for Drug Registration (CDR) of the PPB	The Regulatory and Registration Directorate	General Directorate of Medicines, Supplies, & Drugs (DIGEMID)	Division of Drug Registration (Roz)	Drug Control Division of the FDA	General Directorate of Pharma. and Pharmacies (GDPP)	Drug Registration Dept. (DRD) of the NDA	Drug Reg. Dept. (DRD)
Fees	Original: $1,000 Generic: $333 Similar : $333	Original: $2,700-27,000 (dependant on size of manuf.) Generic: $2,000 Similar : $7,000	Import Drug License: $6,600	New drug: $1,200 Import: Production site - $1,500; Product - $1,000	Local: $500 Imported: $1,000	Local: $465* Orphan drug: $166* Imported:[39] $3.3 per app; Prescription - $1,662*; OTC drugs - $6,648*; Orphan drugs - $598*	$89-$100 Note: New 2010 law may change the fee to $1,000	All: 10,000 Note: Products for 'export only' are not required to be registered	Standard Fee: $50[38] Plus charges for other approval process services, determined by FDA	N/A, though registration fees for domestically manufactured and imported products vary	Local: $200 Imported: $500 Partial: $300	Company license: $2,200 Product license: $130

[37] * = + 5% VAT

[38] Charges for services related to licensing, registration, evaluation, and approval processes, including expenses for testing the products, are to be determined by FDA

[39] "Guidelines for prospective agents of foreign manufacturers of regulated products," *Lagos Chamber of Commerce and Industry* Available at: http://www.lagoschamber.com/documents/NAFDAC/COSMETICS%20-%20GENERAL%20GUIDELINES.pdf Accessed 1 July 2010

	Argentina	Brazil	China	India	Kenya	Nigeria[37]	Peru	Russia	Thailand	Turkey	Uganda	Vietnam
Pre-registration lab quality analysis	Yes; for originals and generics Bio-equivalence data not required for 'similars'	Yes; for originals and generics Requires bio-equivalence for generics, but not for 'similars'	Yes; seems to require some pre-clinical studies and quality testing	Yes; for new drugs, pre-clinical and clinical testing info required, including bio-availability and bio-equivalence For imported, stability data, toxicity tests, etc.	Yes; certificate of analysis required	Yes; certificate of analysis required	Yes; GMP certificates and generics bio-equivalence tests	Yes; all results of pre-clinical studies, in addition to results of pharmacological and toxicological tests, and the results of any relevant clinical trials	Preclinical, pharmacology, toxicology, clinical pharmacology and 3 published studies	Yes; bio-equivalence for generics and bio-availability for originals	Requires clinical trial or bio-equivalence data to prove efficacy[40]	Yes; certificate of analysis and stability studies. For new drugs, clinical pharmacology, toxicology reports, bioavailability data, etc. For generics, clinical trial data not critical.
Samples	N/A	N/A	3 samples	Imports: 3 samples	3 samples	3 samples	N/A	Samples required	2 samples	2 samples	2 samples	3 samples
Timeline (Months)	3-4	Original:12-14 Similar: 8-12 Generic: 6-8 Priority: 2.5 Note: If not registered in 180 days, automatically registered	New: 2-3 Import: 18	New: 12-18 Import: 12	Regular: 12 Fast-track: 3	Regular: 3	7 days[41] Note: New 2010 law may change this timeline to 6 months	Local: 6-12 Import: 18 Fast-track: 3	New: 18 Generic: 6-12	7 months	Regular: 3-6 Fast-track: 1-3 New: 12	Regular: 6

[40] Mubangizi D, Kidde S, Tetteh G. "Strategies for Implementation of the New Antimalarial Drug Policy in Uganda: Workshop Report, Entebbe, October 4–5, 2006," *Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health* (2007) Available at: http://pdf.usaid.gov/pdf_docs/PNADI692.pdf Accessed 20 September 2010

[41] "Multisource drug policies in Latin America: survey of 10 countries," *World Health Organization* (January 2005) Available at: http://www.who.int/bulletin/volumes/83/1/64.pdf Accessed 2 July 2010

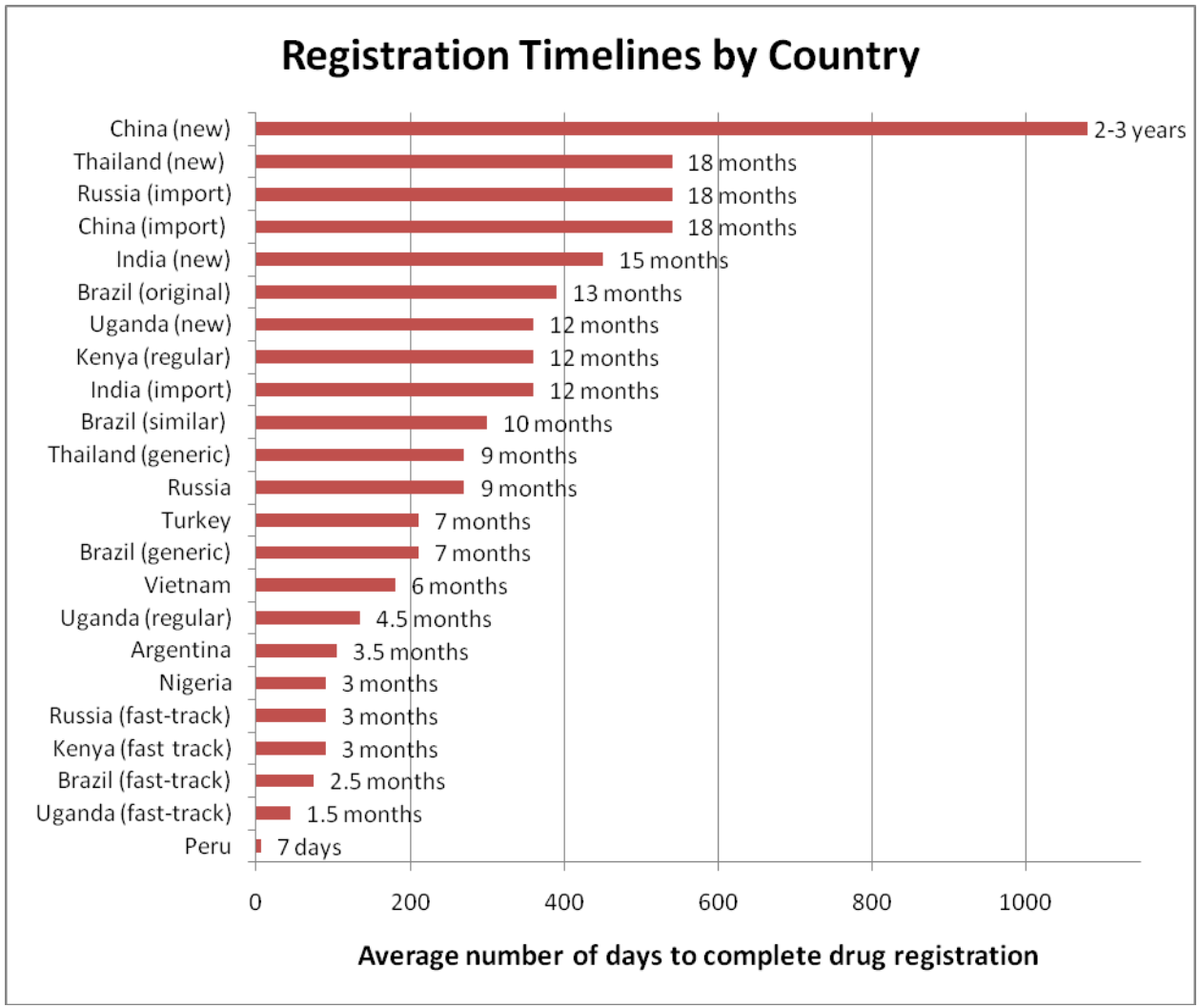
	Argentina	Brazil	China	India	Kenya	Nigeria[37]	Peru	Russia	Thailand	Turkey	Uganda	Vietnam
Validity	5 years	5 years	5 years	3 years	5 years	5 years	5 years[42]	5 years	Indefinite Pre-1983 was valid for 5 years	5 years	N/A	5 yrs – imported & in high demand 3 yrs – imported product not in high demand
Renewal	N/A	Application must be submitted during the first 6 months of the last year of registration Requires payment of Sanitary Surveillance Inspection Fee, or proof of exemption Resubmit packaging, etc. and any changes in the	App. for re-registration is due 6 months before expiry date of initial registration Must resubmit relevant data according to drug regulatory dept. under the State Council	$32.29 for license renewal (if prior to expiry date) $32.29 + $10.76 per month (if within 6 months of expiry date)	Local : $300 - Takes 3 months to complete - Renewal good for 5 years	Fees[43,44] Renewal Form - $3.30 Imported Drugs: Prescription - 1,662*;	Re-registration application must be submitted 60 days before expiration date	In the event of re-registration, drug is granted open-ended certificate	Renewal not required	Renewal application must be submitted to the MOH at least 6 months prior to the expiration date of initial registration	Requires NDA inspections every 3 years	N/A

[42] "Drugs and Pharmaceuticals" (September 2005) Available at: http://www.quiminet.com/estm/files/farma_peru.pdf Accessed 20 September 2010
[43] "Guidelines for prospective agents of foreign manufacturers of regulated products," *Lagos Chamber of Commerce and Industry* Available at: http://www.lagoschamber.com/documents/NAFDAC/COSMETICS%20-%20GENERAL%20GUIDELINES.pdf Accessed 1 July 2010
[44] "Guidelines for Renewal of Imported Registered Regulated Products," *NAFDAC Directorate of Registration and Regulatory Affairs* Available at: http://www.nafdac.gov.ng/guideline?start=20 Accessed 6 July 2010

	Argentina	Brazil	China	India	Kenya	Nigeria[37]	Peru	Russia	Thailand	Turkey	Uganda	Vietnam
		production process since initial registration			- cGMP inspection is required	OTC drug - $3,989* Imported from ECOWAS: Prescription - $831*; OTC drug - $1,662* Domestic Drugs: $232 Late renewal fee: $332* - Timeline: 35 work days - cGMP inspection required						
GMP Inspection	N/A	Yes, Sanitary Surveillance Inspection required	Yes	Yes	Yes, or requires a site master file from plants not inspected or approved by the PPB	Yes, NADFAC inspections required	N/A	GMP compliance required by 2014	Yes	N/A	Requires NDA inspection. Repeated every 3 years. Mandatory analysis of each batch of imported antimalarial meds, anti-TB meds, antiretroviral meds (ARV), and condoms	Yes required; DPM grants GMP certificate which is valid for 2 years

	Argentina	Brazil	China	India	Kenya	Nigeria[37]	Peru	Russia	Thailand	Turkey	Uganda	Vietnam
GMP Fee	N/A	$18,500	Unclear as to whether there is a fee or not	As of October 2009, applying for a GMP certificate is free	Requires a fee to be submitted with app.	Fee of $467.13* to cover processing of application, analysis and license Local: $66.4*	N/A	N/A	N/A	N/A	Provides free testing for the first 3 batches of shipment Additional batches cost is .5% VAT	N/A
Fast-track	N/A	Yes: - If no generic alternative available - New generic imports, provided that companies supply GMP certificates issued by authorities in the US, Canada or the EU	Yes: -Fast track clinical trial approval -New drugs with high efficacy for AIDS, tumors, and rare diseases - Drugs for diseases with no existing treatments	Yes: -Decisions are based on demand for the drug and in public interest	Yes: - Drugs locally made in Kenya - Drugs proven to be more effective than already registered products - No other drug for a certain disease exists	N/A	N/A	Yes: - drugs that differ only in excipients or production tech. from already registered drugs	Yes: - Drugs for major public health problems or life threatening diseases (ex. TB drugs)	N/A	Yes: - ARVs are prioritized and fast-track is available for this class of drugs	N/A

Figure 1:


Registration Timelines by Country
China (new)
Thailand (new)
Russia (import)
China (import)
India (new)
Brazil (original)
Uganda (new)
Kenya (regular)
India (import)
Brazil (similar)
Thailand (generic)
Russia
Turkey
Brazil (generic)
Vietnam
Uganda (regular)
Argentina
Nigeria
Russia (fast-track)
Kenya (fast track)
Brazil (fast-track)
Uganda (fast-track)
Peru
2-3 years
18 months
18 months
18 months
15 months
13 months
12 months
12 months
12 months
10 months
9 months
9 months
7 months
7 months
6 months
4.5 months
3.5 months
3 months
3 months
3 months
2.5 months
1.5 months
7 days
0
200
400
600
800
1000
Average number of days to complete drug registration