

**Testimony before the U.S.-China Economic and Security Review Commission
Hearing on China's Healthcare Sector, Drug Safety, and the U.S.-China Trade in Medical
Products**

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Ginger Zhe Jin

Professor of Economics, University of Maryland, College Park

Research Associate, National Bureau of Economic Research

jin@econ.umd.edu, <http://kuafu.umd.edu/~ginger/>.

Medical products are a classical example of asymmetric information: the seller of medical products tend to have better information about product quality than the buyer, and this information asymmetry can lead to market failures. Medical products are also a special case that differs from other products, partly because consumers may remain in the dark about product quality after consuming the product, partly because poor-quality medical products can have adverse consequences on not only consumers but also those who do not consume the products (via contagion or drug resistance).

1. The problem of poor-quality drugs

Research in this area is frustrated by the lack of a standard definition of counterfeit, fake, falsified, and substandard drugs. According to the World Health Organization, counterfeit drugs refer to drugs that infringe the intellectual property (IP) rights of other legal drugs (trade marks, patents, copyrights, etc.).¹ In other words, counterfeit drugs emphasize IP infringement and the intent to deceive, rather than the drug's chemical content or public health consequences. However, the potential public health danger of poor-quality drugs can be arguably larger than that of IP infringements.

In an original study that is forthcoming in the Journal of Economic & Management Strategy [1], we focus on testing a drug sample's active pharmaceutical ingredients instead of its intent to deceive, and therefore avoid discerning whether a drug sample is counterfeit or not. We define a drug sample as "falsified" if we could not find any significant presence of the correct active ingredient. A drug sample is defined as substandard if it has some but less than 80% of the correct active ingredient. In our study, we obtained 1437 samples of Ciprofloxacin (Cipro) from 22 cities in 18 low-to-medium-income countries and found 59 (or 4.1%) being falsified and 83 (or 5.8%) being substandard. In comparison, visual inspection only identifies 11 problematic samples and all of them turn out to fail the active ingredient test.

These estimates are likely to understate the problem of poor quality drugs in the global market. Because our samples were drawn from pharmacies with a physical storefront in urban areas, we miss mobile kiosks, bus vendors, and other retail channels that could be more dangerous. Moreover, our test focuses on active ingredients only (due to limited resources), so we may have missed problems in impurity, degradation or inactive ingredients. Also, our samples come from consumer-oriented retail markets, which are the end of the whole drug distribution

¹ <http://www.who.int/medicines/services/counterfeit/overview/en/>, accessed on March 26, 2014.

system. Problems seen in our sample could be driven by any part of the manufacturing or distribution process, and it is difficult to pin down the exact source of the problem. That being said, a falsified drug that claims to be Cipro but has no correct active ingredients of Cipro should reflect deliberate cheating. Insufficient active ingredients in substandard drugs can be a result of intentional cheating or non-intentional negligence.

About half of our drug samples claim to be produced in a country that is different from the country in which we purchased the drug. We call them “imports”. The percent of imports in falsified or substandard drugs is similar to the percent of imports in the full sample. Based on the claimed country of manufacturing, we see a lower percentage of failures in “US” or “European” products than products from “Africa”, “China” or “India”. Note that it is difficult to tell whether the claimed country of manufacturing is the actual country of manufacturing, as counterfeiters pay great attention to mimicking the package.

2. How do drug quality regulators and consumers deal with drug quality problem?

Local drug regulators can deal with drug quality problems in several dimensions. They can regulate drug manufacturing by licensing the firm, inspecting the plant, and registering the product. They can regulate drug distributors by licensing personnel and inspecting stores. They may also monitor the market directly, for example by sampling drugs from pharmacies, and try to trace problems back to manufacturing and distribution. Depending on local laws, regulators may have the authority to suspend licenses, impose fines, and/or close down manufacturing/distributing firms. In suspicion of criminal activities, they can collaborate with police and prosecutors and file lawsuits.

In our JEMS study, we correlate whether a drug sample is falsified or substandard to several regulation variables. The first set of regulatory variables focus on whether the sampled brand has been registered by local governments, whether the brand has been prequalified by the WHO, and whether the drug has been approved by a western country with stringent standard (referred to as SRA approved). The other regulation variables include whether a country has any regulation on drug price, and the maximum penalty for drug counterfeiters as stated in the local law.

Among these regulatory variables, we find that product registration is a significant predictor of passing our test of active ingredient. WHO prequalification or SRA approval have no extra effect on passing the test, probably because our definition of “passing” is crude and all the WHO-prequalified or SRA-approved drugs are also registered with the local government. Price regulation or penalty of counterfeiters does not have a significant correlation with drug quality outcomes once we control for product registration. These statistical correlations suggest that product registration with local governments may be an important tool to deal with the drug quality problem by our crude definition. Nevertheless, this suggestion should be taken with caution, as we also find that falsified drugs are more likely to appear as registered products than substandard drugs. One interpretation is that falsified products attempt to mimic registered products in order to increase consumer confidence and/or charge higher price. This finding blurs the signal value of product registration.

To what extent can sophisticated consumers discern drug quality problems? In our JEMS study, we asked our covert shoppers to report their subjective impression of the sampled pharmacy, we also coded each pharmacy's chain status and the transaction prices we paid. Drug samples from a pharmacy that looks decent and affiliates with a chain are more likely to pass our active ingredient test. The price of passing drugs is on average higher than the price of failing drugs, but after we control for other factors, only substandard drugs are priced lower than passing drugs by about 10%; falsified drugs are priced roughly the same as passing drugs.

Our findings highlight the sophistication of deliberate cheaters. They tend to target less on the brand name drugs produced by the original innovators, although the innovator brand is typically much more expensive than generic versions. This is probably because the innovator brand invests more in detecting counterfeits. In our sample, those who falsified the drug with zero active ingredients tend to target well-known generic brands that have already registered with local authorities. Because locally registered products enjoy a significant price premium and registered products are less likely to be examined by inspectors, this targeting strategy makes economic sense. By appearing the same on the package and charging the same price as the authentic version, falsified drugs dupe consumers in both price and quality.

3. Chinese exports of medical products

China exports of medical products fall into three categories: Chinese medicine, western medicine, and medical equipment & device. For both Chinese medicine and western medicine, the majority of Chinese exports are ingredients rather than final pharmaceutical products ready for human consumption.

United States is China's biggest trading partner on medical products. Exports from China may end up in the US as pharmaceutical ingredients for US domestic production, or as imports of final pharmaceutical products. The source of ingredients is almost always hidden from end consumers, sometimes even the final drug manufacturers have a hard time tracing down the ultimate source of ingredients. Even if Chinese exports come as final products and from a legitimate source, they may not appear as "made in China" in the eyes of end consumers as medical products are often repackaged and resold as they move along the global supply chain. Chinese exports from illegitimate sources are even less constrained, as they can pretend to be from anything from anywhere.

The relationship between Chinese producers and the rest of the global supply chain is more complicated than simply being the two sides of the trade. According to a news article that cites numbers from the Chinese customs², over 29,000 Chinese enterprises have engaged in exporting health products out of China in 2013. About 18% of them are foreign-funded to some extent, and they account for close to 37% of the total export value. Some of the Chinese exports to the US may be produced by US company's manufacturing plants in China. For example, Pfizer has invested \$1 billion, employed 9000 employees, and set up 4 manufacturing

² http://www.menet.com.cn/Articles/information/201402/201402191458575857_109526.shtml, accessed on March 26, 2014.

facilities in China since 1980.³ Foreign-funded enterprises also import large numbers of health products into China, mainly in the form of finished products of western medicine and medical equipment/device.

4. Challenges facing Chinese regulators

Recently, Chinese government has shown a determination to impose harsher regulations on medical products. However, there are many challenges on the way.

First of all, China has a large population, enormous heterogeneity, and a relatively diverse system of production and distribution for medical products. According to the National Bureau of Statistics of China, 630 million (or 46.27%) people live in rural areas in 2013. It is usually more difficult to ensure drug access and drug quality in rural areas than in urban areas. Some of the stated goals of the eleventh five-year plan (2006-2010) are to ensure a better coverage of drug monitoring and drug access in rural areas. The diverse production and distribution system also contributes to the difficulty of drug quality monitoring. According to a 2011 annual report from the Chinese government, over 6000 Chinese firms are involved in manufacturing health products, about 4000 of them are related to either Chinese or Western medicine.⁴ An online report from a major financial analyst estimates that more than 400,000 retail stores sell medicine in China up to date.⁵ Even if Chinese government is willing to adopt stringent laws, it is very difficult to enforce high quality practice across a large number of small manufacturers, distributors and retailers. It is not uncommon to observe retail pharmacies selling prescription drugs without prescription or selling without licensed pharmacist in store, although both have been required under a 1999 regulation.

China has made some progress in cracking down bad players in the market of medical products. During the five-year period from 2006 to 2010, China has identified 1.49 million legal violations and revoked 47,798 unlicensed operators in the area of pharmaceutical products, medical equipment, and medical devices. These cases involve roughly 400 million US dollars.⁶ It is difficult to tell whether these detected problems account for a large or small proportion of all the misbehavior prevalent in China.

The second challenge facing Chinese regulators is China's hierarchy structure of administration. Given the size of China, it is inevitable to have multiple levels of governments. Each level of the government may have multiple departments related to food and drug safety, ranging from the National Health and Family Planning Commission (the former Ministry of Health), the China Food and Drug Administration (CFDA), to the National Development and Reform Commission, and the Ministry of Human Resources and Social Security. (There are also non-administrative units such as the China Association of Pharmaceutical Commerce.) Not only is it complicated to define who is responsible for what, it is but also challenging to coordinate between departments across different levels of the government. To address the problem, in March 2013,

³ http://www.pfizer.com.cn/pfizer-china/about_pfizer_china_en.aspx, accessed March 26, 2014.

⁴ The 2011 Annual Report of Health and Medical Statistics of China (《中国医药统计年报 2011》).

⁵ <http://www.gtja.com/zt/sbyw/sbywContent.jsp?docId=14477949>, accessed on March 26, 2014.

⁶ <http://www.cphi.cn/news/show-18174.html>, accessed on March 26, 2014.

China has set up the CFDA as a ministry-level agency that consolidates authorities in food and drug safety. Still, there could be inefficiency and corruption at different levels of governments. For example, in 2007, the former head of the State Food and Drug Administration (which became part of CFDA after the 2013 consolidation), ZHENG Xiao Yu, was convicted to the death penalty for taking more than 1 million US dollars of bribes or gifts and approving six types of fake medicines in exchange. In 2013, China arrested six government officials in Zhejiang province after local manufacturers were found using an illegal industrial chemical to make drug capsules.⁷

A more fundamental problem of China's political hierarchy is that it introduces incentives to ignore or hide quality problems. Local government officials are appointed from the top, and GDP growth is one the most salient measures of performance when they are considered for promotion. Given the high value of medical products, firms producing or distributing medical products may be a good contributor to local GDP and therefore enjoy relaxed monitoring from local governments. Furthermore, local officials have incentives to stifle any public exposure of quality problems. Whistleblowers, activists, and victims are discouraged from exposing quality problems on newspapers, TVs, and the Internet. They can be even harassed and jailed for disrespecting the government. The lack of incentives to discover and solve problems has contributed to scandals in many industries. For example, the 2008 Chinese milk contamination has caused at least four infant deaths, 53,000 hospitalizations⁸, and an estimate of 300,000 victims.⁹ It is widely believed that lack of government's safety monitoring is an important factor underlying the scandal.

In addition to market fragmentation and political hierarchy, a subtler but potentially more challenging issue is how to strike a balance between drug quality and drug affordability. In the US, prescription drug expenditure accounts for roughly 9.4% of all health expenditure.¹⁰ It is difficult to get a corresponding number for China, but a recent article of The Economist¹¹ claims that "China's spending on medicines is 40% of total health expenditure, far higher than the average for OECD countries, of 16%." This is partly because China regulates diagnosis and non-drug treatments at a low level of price, which motivates hospitals to use drug sales to cross-subsidize diagnosis and non-drug treatments. Unlike in the US, hospitals are the main health care providers in China; they are also the main retail outlet for patients to access prescription drugs. Hospitals can achieve higher prescription drug sales by prescribing more drugs or raising the unit price of each prescription drug. Because brand name drugs are sold at higher prices and usually imply higher profit margins than generic prices, hospitals have an incentive to sell brand name drugs instead of the generic version of the same drug. The high price and high

⁷ <http://www.bloomberg.com/news/2013-03-10/china-plans-to-elevate-food-drug-regulator-to-ensure-safety.html>, accessed on March 26, 2014.

⁸ <http://www.nbcnews.com/id/26827110/#.UzScPEJdXgU>, accessed on March 26, 2014.

⁹ <http://www.theguardian.com/world/2008/dec/02/china>, accessed on March 26, 2014.

¹⁰ National health expenditure 2012 highlights from the Centers for Medicare & Medicaid Services, available at <http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/downloads/highlights.pdf>, accessed on March 26, 2014.

¹¹ <http://www.economist.com/news/china/21595431-medicines-are-over-prescribed-and-overpriced-physician-heal-thyself>, accessed on March 26, 2014.

demand for prescription drugs, together with imperfect quality monitoring, motivate both counterfeits and substandard drugs.

Ironically, tougher quality regulations may have the potential to worsen the drug quality problem. When the government introduces more drug safety regulations, it may increase the total cost of good-quality drugs. The increased cost is probably not hard to absorb by brand name drugs, because brand name drugs already have a good profit margin to buffer the cost and the demand for brand name drugs is less elastic as patients often believe brand name drugs to have a higher quality. In comparison, the extra cost of drug regulation may squeeze the narrow profit margin of generic drugs and pressure generic drug manufacturers to cut corners. As a result, tougher drug safety regulations may introduce a danger to push up drug prices and sometimes even worsen the quality of generic drugs that are accessible and affordable to patients with limited resources. To make things worse, higher drug prices attract outright cheaters even more, as they are not subject to the extra regulatory cost but have the freedom to mimic high-price drugs. This danger is more real, if extra regulations trigger more bureaucratic costs but bring little improvement in detecting and solving quality problems.

It is worth noting that the tension between drug safety and drug affordability is not unique to China, many developing countries face a similar problem. This is probably why we observe distinctive patterns between falsified and substandard drugs in our own study: falsified drugs have fewer active ingredients than substandard drugs but they charge almost the same price as passing drugs while substandard drugs are 10% cheaper.

5. Potential solutions

The recent report from the Institutes of Medicine (IOM) [2] has made a number of suggestions to improve drug safety, including clarifying the definition of counterfeit and substandard drugs, increasing pharmacovigilance, adopting a track and trace system, strengthening wholesale licensing, training regulators, and standardizing an international code of practice.

I agree with most recommendations from the IOM. It is important to realize that the drug safety problem in the international market is much broader than protecting intellectual property rights. Unsafe drugs have adverse consequences for public health, they are also related to drug access and drug affordability. Clarifying the definition of counterfeit and substandard drugs is the first step to distinguish intellectual property issues from the public health aspects of drug safety.

Governments in different countries may have good reasons to adopt different regulations in drug safety, but the world is flat, especially in high-value products like prescription drugs. Manufacturers have strong economic incentives to obtain cheaper ingredients from developing countries and/or shift manufacturing capacity to low-cost places around the globe. It is important to set up an international code of practice and enforce it effectively. I am not sure how to achieve this, one way is to strengthen collaboration between the central governments of various countries and find a way for each central government to effectively enforce the international standard within its country. Another way is to strengthen product liability law and clarify the responsibility of each player in the production and distribution system. If a product is

found problematic under a US manufacturer, the manufacturer should be responsible for the problem even if the source of the problem comes from an international supplier of some pharmaceutical ingredients. This way, the manufacturer will have incentive to monitor the quality of ingredient suppliers, and ingredient suppliers will have incentive to obtain high quality ingredients. A track and trace system will also help in clarifying and enforcing the responsibility of each player in the production and distribution process.

6. Recommendations to the US Congress

More specifically, I would recommend the US congress to consider the following actions in strengthening medical product quality:

First and foremost, find out how serious the problem is. It is amazing how little we know about the extent of drug safety and drug quality problems around the world. We probably know even less about quality problems in medical equipment and medical devices. The process of problem discovery should involve both government and non-government efforts. More research funds, from both public and private sources, are needed to support systematic research in this area.

Secondly, it is crucial for drug manufacturers and drug distributors to play a more active role in drug quality. To what extent and in which format has the manufacturing process been outsourced? What is allowed and what is not allowed on both ends of the outsourcing process? Who is responsible for which part of the manufacturing and distribution process? What information should be gathered and subject to whose scrutiny and when? What liability does each player have if a problem arises? Answers to these questions will require international collaboration between governments, manufacturers and distributors, with the technology of internationally tracking and tracing medical products.

Lastly, medical product quality should not be considered in isolation. Extra regulations on product safety, in and out of the US, will likely increase the cost of prescription drugs, which may add burden on end consumers. The balance between drug affordability and drug quality is not only important for developing countries but also relevant for US consumers. Our study of the online prescription drug market [3] shows that many US consumers, especially the elderly and near-elderly, are concerned with prescription drug cost and they are willing to purchase from foreign pharmacies even if this is highly discouraged by the FDA. Our study also shows that private certification of foreign pharmacies does provide value for consumers trying to distinguish among Internet pharmacies. Imposing more drug safety regulations without consideration of prescription drug cost will likely upset price-sensitive consumers and worsen the tension between drug cost and drug quality. Equally important, one must consider the efficiency of enforcing drug safety regulations. Is it most efficient for the FDA of US to police all the ingredient plants of China? Should the US coordinate with other large medical product markets (e.g. European countries, Canada, India, China and Brazil) in good manufacturing and good retail practice standards? Can academic, private or other government resources be used in this process? These questions should be examined in depth before the US commits to an overhaul of its regulatory system on medical product quality.

Citations:

[1] Roger Bate, Ginger Zhe Jin, and Aparna Mathur “Falsified or Substandard? Assessing Price and Non-Price Signals of Drug Quality”, forthcoming Journal of Economics & Management Strategy, available at <http://kuafu.umd.edu/~ginger/research/BJM-falsified-substandard-JEMS-final-01222014.docx>, also available as NBER working paper #18073.

[2] Institutes of Medicine, “Countering the Problem of Falsified and Substandard Drugs”, published by the National Academies Press (2013), available at http://www.nap.edu/catalog.php?record_id=18272.

[3] Roger Bate, Ginger Zhe Jin, and Aparna Mathur “In Whom We Trust: The Role of Certification Agencies in Online Drug Markets”, the B.E. Journal of Economic Analysis and Policy, Volume 14, Issue 1 (Dec 2013). Available at <http://www.degruyter.com/view/i/bejeap.2014.14.issue-1/bejeap-2013-0085/bejeap-2013-0085.xml?format=INT>.