



Bad Medicine in the Market

By Roger Bate and Kathryn Boateng

Counterfeit medicines are an insidious threat to global health, and the risks they pose have been largely underestimated to date. Apart from failing to cure disease, they can cause mental and physical damage—and even death. Fake drugs containing insufficient active ingredients breed resistance, which can make standard drugs useless. No area of the world is unaffected, but mounting evidence shows that the problem is disproportionately severe in developing and emerging-market countries, which also have the highest burden of infectious diseases. Countries have the primary responsibility—both in stopping criminal manufacturing and distribution and in protecting their citizens from counterfeit products—but multilateral organizations such as the World Health Organization (WHO) must do more to expose the problem and help countries tighten regulatory controls. While monitoring of outright fakes is improving and arrests of those trading in them are increasing, some global agencies are promoting drugs they assume to be good copies of branded drugs but which are probably substandard. Global agencies must stop this double standard and develop effective methods of improving detection of all substandard products.

What constitutes a “counterfeit” drug varies from country to country. WHO broadly defines a fake or counterfeit drug as “a medicine which is deliberately and fraudulently mislabeled with respect to identity and source. Counterfeiting can apply to both branded and generic products, and may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.”¹ For the most part, “originator pharmaceuticals,” also known as branded pharmaceuticals, are the main target of counterfeiters, since they promise high profit margins.

As with any illegal activity, the scope of the problem is impossible to define with precision. Unofficial estimates from researchers on the proportion of counterfeit drugs in the pharmaceutical market range from a high of 50 percent to a low of 1 percent, with other estimates from reputable researchers at 40, 30, and 17 percent.² WHO

reported in 2006 that the fake drug industry has annual revenues of over \$40 billion—a figure sure to increase as more cases of counterfeit drugs are investigated and reported.³ The U.S. Food and Drug Administration (FDA) reports that the number of open investigations into domestic counterfeit drugs jumped from about five per year in the 1990s to more than twenty by 2000;⁴ in 2004 alone, there were fifty-eight documented investigations.⁵ WHO cites the Center for Medicine in the Public Interest’s prediction that counterfeit drug sales will reach \$75 billion globally in 2010—an increase of more than 90 percent from 2005.⁶

This Rolex Might Kill You

Counterfeit drugs are commonly made and distributed by criminal gangs, who are attracted by the high profit margins of the trade.⁷ Many counterfeiters use fake Western addresses to impress patients and doctors in poor countries.⁸ These gangs also peddle other illicit items, such as narcotics, arms, and fake jewelry. Like fake Rolexes, fake drugs are

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often hard to identify. A fake Rolex will probably tell time, but when it does not, anyone can tell it is a fake. The ineffectiveness of fake drugs may be revealed only when a life has been put at risk. Fake drugs also undermine confidence in branded products and even entire health-care systems.

Yet counterfeiting pharmaceuticals usually carries far lower penalties than producing and selling narcotics—and it is becoming just as lucrative and is therefore a booming business. The extent of the problem is shocking: counterfeit drugs manufactured by South American narcotics gangs or unregistered chemical works in China have infiltrated legitimate supply chains and ended up in pharmacies, clinics, and hospitals all over the world. Even CVS and Rite Aid have been fooled.⁹

Counterfeit drugs contain little or none of the active ingredients of legitimate drugs, with varying consequences depending on the disease. An outright lack of therapeutic benefits may cause death, particularly in infants. But low-strength medicines will only knock out the weaker diseases, leaving the stronger ones to thrive and develop resistance to the drug. This means that even the genuine drug will be rendered useless to the patient; unless he can get access to vastly more expensive second-line drugs, he has no hope. If the disease develops population-level resistance, a whole drug class will be lost. In some cases, toxic ingredients from fake drugs have caused death outright.¹⁰ Dora Akunyili, the director general of the Nigerian National Agency for Food and Drug Administration and Control, astutely analyzes the situation in her country and elsewhere: “The evil of fake drugs is worse than the combined scourge of malaria and HIV/AIDS put together. . . . Whereas HIV/AIDS can be avoided, and malaria can be prevented, fake drugs kill en masse, and anyone can be a victim.”¹¹

Tracking Counterfeit Medicines around the Globe

The problem of counterfeiting drugs is rampant in both developed and developing countries. In wealthier developed countries, counterfeiting most frequently affects “lifestyle drugs” such as hormones, steroids, erectile dysfunction, and anti-allergy medicines. In the 1990s,

several deaths associated with the use of a fake version of the antibiotic gentamicin occurred in the United States. More recently, in May 2003, nearly 20 million doses of fake Lipitor, a cholesterol-lowering medication, had to be pulled from U.S. pharmacies.¹² Altogether, because

wealthy countries have stricter regulatory mechanisms, and since most patients in wealthy countries can afford branded medicines, counterfeits account for less than 1 percent of the market value—although 50 percent of Internet sales are estimated to be counterfeit.¹³

In developing countries, the scale of the problem is disproportionately worse. The latest joint estimates by WHO, the Organisation for Economic Co-operation and Development, and the Pharmaceutical Security Institute show that more than 30 percent of medicines in some areas of Latin America, Southeast Asia, and sub-Saharan Africa are counterfeit.¹⁴

For Africa, data are scarcer, but the situation is similarly bad. In 2005, a random survey by Kenya's National Quality Control Laboratories and the Pharmacy and Poisons Board found that almost 30 percent of the drugs in Kenya were counterfeit. Some of the drugs were no more than chalk or water.¹⁵

In poor countries, essential and life-saving drugs used to treat infectious disease such as tuberculosis and malaria are often the drugs under threat.¹⁶ Since the burden of these diseases is greatest in these countries, there is often a frantic demand spurring the sale of counterfeit drugs on the black market despite poor quality and even appearance.¹⁷ The best therapies can be relatively expensive, so—in our anecdotal experience—poor family members of the very sick often buy anything they can afford rather than do nothing.

A field survey from 2002 to 2003 showed that 53 percent of artemisinin-based antimalarials—the most effective treatment available—bought in several Southeast Asian countries were counterfeit and contained incorrect levels of the active ingredient.¹⁸ The authors noted that the problem seemed to have increased significantly compared with their previous survey in 1999–2000.¹⁹

Researchers conducted a quality-control study of anti-malarial tablet samples purchased on the black market in Angola, Burundi, and the Democratic Republic of the Congo.²⁰ The results identify a variety of problems with the drug: dubious packaging, low content of the active

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ingredient, and substandard technological properties (including very low dissolution profiles). In a 2003 survey to determine the quantities of counterfeit antimalarial drugs in seven African countries, researchers found that the active ingredient content in at least one of the three formulations of the drugs tested in all the surveyed countries was below the minimum level recommended for the product.²¹

HIV/AIDS and bird flu treatments are also being jeopardized. In a 2004 study, one researcher discovered counterfeit antiretrovirals (stavudine-lamivudine-nevirapine and lamivudine-zidovudine) in central Africa. This is alarming because the previously effective first-line therapy for treating HIV could soon be rendered defunct due to the development of drug resistant forms. The bird flu scare led to an increased demand for the antiviral drug Tamiflu, one of the proven remedies for the disease. Soon thereafter, fake versions of the drug were flooding the Internet.²²

Developing countries are not only markets for counterfeit drugs—they also produce the fakes, according to a report from the International Policy Network (IPN).²³ The chief culprits are Asian countries like China and India, where oversight is weakest. China had five hundred illegal medicine factories in 2001, a number which has since increased. According to the IPN report, about 15,000 manufacturers of copies operate in India, and while the majority are legitimate (even if their drugs are substandard), “a small minority are ‘fly-by-night’ operations that do not comply with proper regulatory standards.”²⁴ Most of the counterfeit medicines in Nigeria, for example, originate in India, which led the authorities to threaten to ban the import of all drugs from India in 2003. With an influx of legitimate Chinese investment in Africa, however, informed sources say that China may soon take the lead in this odious contest. The manufacture of fake medicines also flourishes in Latin American countries like Argentina, Brazil, Mexico, and Venezuela.

The production of counterfeit medicine often occurs through a “multi-national chain of production and sale” that originates in countries that either do not recognize or loosely enforce patent laws, where the drugs can be synthesized or their component parts bought.²⁵ A copy manufacturer operating in Argentina, Greece, or Mexico purchases the ingredients from a country such as India or Thailand, then presses the tablets or makes the pills and prints counterfeit labels. The fake drugs eventually make their way through several cut-rate brokers to a pharmaceutical distributor.²⁶ These findings suggest that massive

amounts of fake drugs are circulating in drug distribution chains. Even more worrisome, many patients are taking incorrect doses or compositions of drugs—with potentially lethal outcomes.

Cashing In on Death

In studies all over the world, counterfeit medicines, which contain little or no active ingredients, have no therapeutic benefits to patients.²⁷ During the Niger meningitis epidemic of 1995, for example, 2,500 people died as a result of fake vaccines.²⁸ In Haiti, Nigeria, Bangladesh, India, and Argentina, more than 500 patients (mostly children) died after ingesting diethylene glycol (a chemical commonly used as antifreeze) offered as paracetamol syrup.²⁹ Today, due in part to lax regulatory standards, we are seeing contaminated products from China containing the same ingredient.

WHO estimates that 1 million deaths occur from malaria every year. It is logical to conclude that this chilling estimate could be significantly reduced if the medicines available were effective, of good quality, and used correctly. One article notes that an astonishing 200,000 malaria deaths per year would be prevented absent fakes.³⁰ In 1999, at least thirty people died in Cambodia after taking counterfeit antimalarials prepared with sulphadoxine-pyrimethamine (an older, less effective antimalarial), which were sold as the more advanced artesunate.³¹ A study conducted in Southeast Asia in 2001 revealed that 38 percent of 104 antimalarial drugs on sale in pharmacies did not contain any active ingredients and had led to several preventable deaths.³²

Perhaps one of the most worrying implications of the counterfeit boom is the acceleration of new, drug-resistant pathogens, parasites, and bacteria. The IPN report found this especially true of malaria and HIV/AIDS. Scientists have begun to observe resistant strains of bird flu, which could indicate that fakes are already penetrating. The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) says that “drug resistance resulting from the use of counterfeit medicines is among key factors contributing to the upsurge of major infectious diseases in developing countries.”³³

Aside from their hefty death toll, counterfeit drugs undermine incentives to invest in further research and development. The use of fake drugs also undermines confidence in health-care systems, health professionals, pharmaceutical manufacturers, and distributors. It deprives

pharmaceutical companies of significant financial resources and places financial burdens on patients and governments with two major consequences: money is wasted on drugs that do not work, and additional funds must be spent on purchasing genuine products to deal with the ensuing devastation that toxic or under-strength products cause. This is particularly damaging in developing countries, where disposable income for health care is significantly constrained.

Fighting Counterfeit Drugs

Since its inception in 1946, WHO has often attempted to quell the spread of counterfeit drugs. Article 2 of the WHO constitution establishes its obligation to set standards through its Quality Assurance Program. WHO initiated programs for the prevention and detection of counterfeit drugs, and in 1982 established a Counterfeit Drug Database. In 1992, WHO joined forces with IFPMA to settle on a working definition of a counterfeit drug. More recently, in 2000, WHO convened a working group on drug quality and counterfeiting. Made up of WHO officials and organizations representing patients, pharmacists, and medical professionals, the group hopes to raise awareness about the problem of counterfeiting while promoting effective regulatory safeguards to ensure that patients are protected from the hazardous effects of these medications.³⁴ Currently, WHO is also advancing a proposal to establish an International Medical Products Anti-Counterfeiting Taskforce, which will mobilize resources.³⁵

At the national level, some countries are taking steps to tackle this problem. Nigeria, which has a major problem with counterfeits, issues bulletins and maintains a website with information on counterfeit drugs and food to educate consumers. In 1996, the Philippines enacted a law allowing for random sampling and monitoring of the drug quality in pharmacies and hospitals and punishing offenders with long prison sentences or hefty fines. China, where many products are fraudulently manufactured, has taken the drastic step of sentencing an official in charge of food and drug safety, Zheng Xiaoyu, to death for accepting bribes to approve counterfeit products.³⁶ As the legal literature has demonstrated, increasing the

cost (i.e., judicial sentences) of illegal activity often does not lower the activity significantly, but rather just increases the level of brutality involved.³⁷ While more punitive sentencing for those peddling fake drugs is certainly warranted, it is only part of the solution. Only increasing monitoring activity by technically qualified laboratories combined with concerted policing will lower criminal fake drug activity.

Fighting Substandard Drugs

Although WHO has done much to prevent the spread of fake drugs, it has actually encouraged the use of substandard drugs through the promotion of products it considers to be generics—but which have unverified quality.

Substandard drugs can be more dangerous than fakes since they contain active ingredients, but at sub-lethal levels for the bacteria/parasite, therefore breeding resistance.

As documented in a recent paper,³⁸ this has been a significant problem for HIV drugs. Unfortunately, the Global Fund to Fight AIDS, Tuberculosis and Malaria has exacerbated the problem by not requiring 93 percent of the drugs on its approved antimalarial compliance list to have bioequivalence registration with a competent agency. Most of the drugs purchased are of the approved variety, but sources inform us that nearly 20 percent of total purchases—well over 450 transactions—are for non-approved drugs. European and Indian companies have also exploited loopholes in domestic legislation which allows them to copy drugs for export without undertaking significant quality testing. Belgium and Italy in particular have allowed drugs produced in their countries to compete for Global Fund awards without having them tested.³⁹

It is uncertain how damaging substandard, pseudo-generic drugs may be for patient safety. Their use—and hence impact—is set to grow even faster than the market for fake drugs. This is disquieting, since the Global Fund does not see this as a problem. It continues to use funds from the Bill and Melinda Gates Foundation and the G8 countries to purchase such drugs. The Global Fund mistakenly assumes that because the drugs are cheaper, more lives will be saved, which is only true if the copies are as good as the originals. Meanwhile, the Fund continues to show antipathy toward the research-based pharmaceutical industry. Board members voted to increase access to antimalarials of unproven quality to prevent Novartis, the producer of the best drug on the

market, from increasing its dominance, even though Novartis sells the drug at lower than cost.⁴⁰

When the new head of the Global Fund was asked about this issue in Washington in May 2007, he brushed the matter off without even acknowledging the seriousness of the problem.⁴¹ Only when tragedy strikes will action be taken. Action is vital because substandard drugs can be more dangerous than fakes—especially at the population level—since they contain active ingredients, but at sub-lethal levels for the bacteria/parasite, therefore breeding resistance.

A final reason to act is that approval of poor copy drugs provides cover for the broader acceptance of total fakes. When doctors and patients are inundated with new copy drugs, it is more difficult for doctors to discern total fakes, making drug policing more complicated and expensive.

Looking Ahead

The problem of counterfeiting requires a concerted effort from all stakeholders. As one top health official from the Philippines noted, “The fight [against counterfeit medicines] is a cooperative undertaking.”⁴² As the IPN paper notes, to contain the global counterfeiting scourge, it is crucial “to address those lacunae of governance which allow LDC counterfeiters to ply their trade with relative impunity.”⁴³ Most importantly, it is essential that intellectual property rights and the rule of law be upheld in the countries where the majority of these drugs are produced. In South American countries, the penalty for illicit cocaine and heroin dealing is fifteen years of jail time. The penalty for the production and sale of fake drugs is only six months, with the perpetrator out in days on bail.⁴⁴ These sentencing incongruities should be rectified. Stiff penalties are needed because counterfeiting offers a high-profit, low-risk trade-off. In 2003, an expert committee in India recommended that the maximum penalty for the sale or manufacture of fake medicines be changed from life imprisonment to the death penalty and that the minimum prison sentence for these offenses be increased from five to ten years.⁴⁵ But as noted above, increasing sentencing without massively increasing policing will have little impact on the fake drug market.

Promoting generics as an alternative to tackling drug counterfeiting is not a viable option unless the necessary recognized international regulatory standards—including bioequivalence—are in place to ensure the quality of products on the market. Unless such standards are set,

aid agencies will continue to exacerbate and tolerate bad medicine in the market.

AEI editorial assistant Evan Sparks worked with Mr. Bate and Ms. Boateng to edit and produce this Health Policy Outlook.

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