

REVIEW ARTICLE

The Health and Economic Effects of Counterfeit Drugs

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Background: Counterfeit drugs comprise an increasing percentage of the US drug market and even a larger percentage in less developed countries. Counterfeit drugs involve both lifesaving and lifestyle drugs.

Objective: To review the health and economic consequences of counterfeit drugs on the US public and on the healthcare system as a whole.

Method: This comprehensive review of the literature encompassed a search of MEDLINE/PubMed, Google Scholar, and ProQuest using the keywords “counterfeit drugs,” “counterfeit medicines,” “fake drugs,” and “fake medicines.” A search of the various FiercePharma daily newsletter series on the health-care market was also conducted. In addition, the US Food and Drug Administration and the World Health Organization websites were reviewed for additional information.

Discussion: The issue of counterfeit drugs has been growing in importance in the United States, with the supply of these counterfeit drugs coming from all over the world. Innovation is important to economic growth and US competitiveness in the global marketplace, and intellectual property protections provide the ability for society to prosper from innovation. Especially important in terms of innovation in healthcare are the pharmaceutical and biopharmaceutical industries. In addition to taking income from consumers and drug companies, counterfeit drugs also pose health hazards to patients, including death. The case of bevacizumab (Avastin) is presented as one recent example. Internet pharmacies, which are often the source of counterfeit drugs, often falsely portray themselves as Canadian, to enhance their consumer acceptance. Adding to the problems are drug shortages, which facilitate access for counterfeits. A long and convoluted supply chain also facilitates counterfeits. In addition, the wholesale market involving numerous firms is a convenient target for counterfeit drugs. Trafficking in counterfeits can be extremely profitable; detection of counterfeits is difficult, and the penalties are modest.

Conclusion: Counterfeit drugs pose a public health hazard, waste consumer income, and reduce the incentive to engage in research and development and innovation. Stronger state licensure supervision of drug suppliers would be helpful. Technological approaches, such as the Radio Frequency Identification devices, should also be considered. Finally, counterfeit drugs may raise concerns among consumers about safety and reduce patient medication adherence.

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Intellectual property represents original, creative works and innovations who belonging to inventors, artists, musicians, and authors who, and businesses that, create something or acquire rights to a creation. The exclusive rights and legal protections of intellectual property come in the form of copyrights, trademarks, and patents. These protections encourage innovation and creativity, but the rewards for innovation and creativity can be undermined by widespread theft associated with counterfeiting and trafficking of pirated goods. The Internet has become an important and convenient means for consumers to shop and save money. However, websites that traffic counterfeit goods have flourished on the

Internet, creating confusion between which sites sell authentic goods and which do not.

When reflecting on counterfeit and pirated goods, knockoff luxury handbags, fake watches, and free music and videos may come to mind. The counterfeiting and pirating of goods may seem to be a victimless crime, where no one is harmed by imitation goods sold at much lower prices than brand-name products. However, the world of counterfeiting and piracy stretches to nearly every product on the market and has often led to considerable harm to consumers, including death. The consequences are well-known, as the Department of Homeland Security states, “counterfeit and pirated goods pose a serious threat to America’s economic vitality, the health and safety of American consumers, and our critical infrastructure and national security.”¹ Piracy and counterfeiting are not victimless crimes; they cost US businesses more than \$200 billion annually and account

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for the loss of more than 750,000 jobs.² This is also a worldwide problem.

Medicines have often been counterfeited, sometimes with dire consequences to patients.³ Counterfeit drugs are a public health issue in the United States and worldwide. The issue of counterfeit drugs has been growing in the United States with the supply of these counterfeit drugs coming from all over the world. Counterfeit drugs not only take income from consumers, by having them pay for products that have little or no medical value, but they can also lead to unresolved health problems, and even death.³ There are various issues involved with counterfeit drugs and reducing their availability. Especially significant, counterfeit drugs may raise concerns among consumers about safety, and may therefore reduce patient adherence.

In this review, we examine how the legitimate supply chain has been infiltrated by counterfeits, as well as the role of the Internet in facilitating the distribution of counterfeit drugs, and the impact on patients, drug innovation, and the pharmaceutical industry.

Counterfeit Medicines

Counterfeit medication is a problem in the United States, and even more so worldwide. Counterfeit medications are a waste of income of patients, and they often endanger the public's health and safety. One case that illustrates this problem is that of a patient who was treated with injections for anemia, after a liver transplant. After 8 weeks of injections, the patient was still not responding to treatment. The treating physicians discovered that the medicine the patient used was counterfeit.⁴ In such cases, the consequences of counterfeits can be serious.⁴

A particularly serious case involved counterfeit versions of bevacizumab (Avastin), a cancer-fighting medication. Avastin's manufacturer, Roche, notified physicians in February 2012 of a counterfeit version of bevacizumab that contained salt and starch, but not the active component of the drug.⁵ Another example of the dangers of counterfeit medications in the United States is the 2008 counterfeit case of the blood thinner heparin. In this case, the active ingredient was replaced with a cheaper substance that caused patients to have adverse reactions and resulted in a nationwide recall of heparin.⁶ The medication, whose counterfeit active ingredient came from China (a major source of counterfeiting), was suspected to be the cause of as many as 81 deaths.⁶ The implications for patients are clear: counterfeits can kill. The US company that sold heparin was subject to 740 lawsuits and eventually sold the division that produced the medicine.⁶

Preventing counterfeit medicines from entering the United States is especially difficult, in part because near-

KEY POINTS

- Counterfeit drugs comprise a growing percentage of the US drug market.
- Drug shortages, a long and convoluted supply chain, and Internet pharmacies are contributing factors.
- US consumers are largely unaware of the dangers of purchasing counterfeit drugs from Internet pharmacies: an estimated 36 million Americans have bought drugs online without a valid prescription.
- This review of the literature investigates the implications of how the legitimate supply chain has been infiltrated by counterfeits.
- Real-world evidence from several cases, including the case of bevacizumab (Avastin), are presented as recent examples of the serious harm drug counterfeiting can cause patients and the cost to manufacturers and drug innovation.
- Controlling the availability of counterfeit drugs is not simple, but necessary, given the serious public health issues they pose.
- The threat to the safety of American patients and drug innovation merit strong sanctions regarding counterfeit drugs.

ly 40% of drugs are made overseas and approximately 80% of the active medicinal components of drugs are imported.⁷ Because many of these medicines are expensive, buyers are attracted by lower prices. The rise of Internet pharmacies makes regulation of drug safety more difficult. Detecting counterfeits is often difficult, because many of these goods pass through a long and complicated distribution network, thereby creating opportunities for counterfeits to enter the legitimate supply chain.

Counterfeit medications are also a worldwide problem. The World Health Organization (WHO) estimates that as much as 30% of the medicines sold in parts of Asia, Africa, and Latin America are counterfeit.⁸ In 2011, 64% of antimalarial drugs in Nigeria were found to be counterfeit.⁹ Worldwide, an estimated 10% of all medicines are counterfeit.¹⁰

Method

This comprehensive review of the literature is based on a search of online databases, including MEDLINE/PubMed, Google Scholar, and ProQuest using the keywords "counterfeit drugs," "counterfeit medicines," "fake drugs," and "fake medicines." A search of the various FiercePharma daily newsletter series related to the health-care industry was also conducted. In addition, the US Food and Drug Administration (FDA) and the WHO websites were reviewed for additional information.

Consumer Issues: Harmful Effects

Patients can experience a variety of problems from the use of counterfeit drugs. The various scenarios depend on the ingredients that make up the counterfeit drug. The first scenario is a counterfeit drug that contains no active ingredient or no harmful ingredients.¹¹ In the case of the counterfeit drug that has no active ingredient, the drug fails to help the patient get better, which can ultimately harm the patient. In the case of antibiotics, for example, this can promote antibiotic resistance and the use of stronger antibiotics, because physicians would believe that the first-line drug was not working, not knowing that the patient had been taking a counterfeit drug.¹¹

A second scenario is that the counterfeit drug has no active ingredient and may have any number of harmful ingredients, including bacteria-laced water, toxic yellow paint, floor wax, colored dye, powdered cement, boric acid, and antifreeze.¹¹ More than 500 children around the world died from counterfeit cough syrup that was tainted with ethylene glycol (ie, antifreeze).¹¹ In another case, counterfeit inhalers for the treatment of pediatric cystic fibrosis were found to contain contaminated bacteria that went directly into the lungs of unsuspecting children.¹² Another case involved patients with cancer who used erythropoietin, in which the counterfeit intravenous drug was diluted with bacterially contaminated water and injected directly into the patients.¹²

Another scenario is that of a wrong drug used in the counterfeit agent. Counterfeit versions of GlaxoSmith-Kline's over-the-counter weight-loss medication orlistat (Alli) have been distributed in the United States. The counterfeit contained the controlled substance sibutramine instead of orlistat.¹³ The FDA reported that this counterfeit version could be dangerous for certain patient populations who unknowingly take it, and could potentially produce harmful interactions with other medications that patients may be taking.¹³

One other scenario involves a counterfeit drug that contains the wrong concentration or wrong dose of the drug. One example of this is the case of a physician who was supplied with a research version of onabotulinumtoxinA (Botox) that was much more concentrated than the real medicine, and is not intended for human use.¹¹ This resulted in respiratory paralysis and near death for several patients, including the physician who was using it himself.¹¹ In general, counterfeit drugs create uncertainty, confusion, and doubts about the value of the real drug and may lead to the use of alternative, less-desirable drugs or therapies.

Supply Issues

Indicative of the concern over supply chain issues, on February 27, 2014, the House Energy & Commerce Sub-

committee on Oversight and Investigations conducted a hearing entitled, "Counterfeit Drugs: Fighting Illegal Supply Chains."¹⁴ Counterfeit drugs are available through the legitimate supply chain, which also includes a small percentage of online pharmacies. The legitimate supply chain has many stages in which counterfeits can enter, starting with providing ingredients for manufacturing of the drug. Subsequent stages for infiltration include storage, transportation, and finally distribution. Approximately 90% of drugs are distributed in the United States by national wholesalers directly to end suppliers that generally include pharmacies, physicians, hospitals, and clinics.¹⁵ However, the remaining 10% can often follow a circuitous route, which increases the risk for counterfeits entering the market.¹⁵

In one instance, counterfeit epoetin alfa (Epoen), which was purchased from a pharmacy, had at least 13 chains of owners and caused considerable health issues for a young patient who had undergone a liver transplant in the United States. In addition to the manufacturer and the major distributor, this drug was handled by 3 different wholesalers, 2 pharmacies, 4 unlicensed go-betweens, and 1 suspected counterfeiter.¹⁵ This case and many others illustrate why decreasing the number of links in the supply chain, in an effort to reduce the counterfeit drug supply, is desirable for the health and safety of patients.

A problem area is the wholesale market, which comprises 3 types of wholesalers—primary wholesalers; several large, regional wholesalers; and many thousands of secondary wholesalers. The primary and large, regional wholesalers interact with the manufacturers, and they are usually not the avenue of entry for counterfeits. Conversely, secondary wholesalers do not deal directly with drug manufacturers, and they buy and sell drugs in response to market shortages and surpluses. In addition, they package and repackage the drugs, which provide an opportunity for counterfeits to enter the market.¹⁶

The issue related to decreasing the number of people and routes in the supply chain must be addressed. One suggestion from the House Energy & Commerce Subcommittee on Oversight and Investigations hearing on counterfeit drugs was to increase state licensure supervision of drug wholesalers: it was noted that state pharmacy boards should exercise more effective supervision of these wholesalers.¹⁶ Another approach is technology-based, which involves establishing a mandatory drug track-and-trace system. This type of tracking system was implemented in Turkey in 2011.¹⁶

On November 28, 2013, President Obama signed the Drug Quality and Security Act into law, which provides for a national track-and-trace system that would allow a specific drug to be followed from the manufacturer to the

pharmacy.¹⁷ This should make it more difficult for counterfeit drugs to enter the legitimate US pharmaceutical supply chain. The law provides for a national system of electronic tracking of drugs and is expected to be implemented by 2015.¹⁷

The technology for the track-and-trace system most likely to be used is the Radio Frequency Identification (RFID) device, which uses information stored and remotely retrieved on transponders to provide automatic identification.¹⁸ An RFID tag is a chip that can be used to provide serial numbers to confirm the identity of a product.¹⁸ International harmonization should be considered to make tracking and tracing more effective.

Another factor exacerbating (or at least contributing to) the problem of counterfeit drugs is the recent shortages of several drugs in the United States.¹⁹ Many of the drugs in short supply are lifesaving anticancer drugs, and this promotes the development of counterfeits that can result in considerable suffering or death for the patient. In the second quarter of 2012, there were 211 drugs associated with shortage issues in the United States.¹⁹ A 2009 case involving ineffective insulin illustrates the problem.²⁰ Patients reported that their insulin was not controlling their blood sugar. The insulin used by these patients had been stolen and was not stored or handled properly, thus losing its potency.²⁰

For drugs in short supply, hospitals and other providers search beyond normal sources to obtain the drugs, increasing the ability of inserting the counterfeits into the market. "Shortages of key medicines in the US and Europe have created new opportunities for illicit traders, while ever-longer manufacturer supply chains open the door to diversion and theft."²¹

Drug shortages lead to increased prices for a legitimate drug and increase the opportunity and ability for unscrupulous people to make financial gains by introducing counterfeit drugs into the market.²⁰ Counterfeiters are able to take advantage of the drug shortage and charge exorbitant prices. Cost markups (presumably compared with standard prices) on drugs associated with shortages during a 2-week period in the beginning of 2011 averaged 650%.²⁰ Particularly high markups, 4533%, were reported for labetalol (cardiology); cytarabine (oncology), 3980%; dexamethasone (oncology, rheumatology), 3857%; and propofol (critical care sedation, surgery), 3161%.²⁰ These shortages sometimes occur because of quality control problems that exist in manufacturing plants, which are then shut down by the FDA.

Internet Pharmacies

Consumers (or patients) in the United States are largely unaware of the dangers of purchasing counterfeit drugs from Internet pharmacies.²² This lack of knowledge

is contributing to what is becoming a major public health issue. In most cases, counterfeit drugs are neither safe nor effective. The use of these drugs can lead to greater sickness, or even to death.

According to a 2009 report, online pharmacy sales were an estimated \$11 billion that year, up from an estimated \$4 billion in 2007.²³ Early on, counterfeit drugs involved primarily so-called lifestyle drugs, especially sildenafil (Viagra), but the market has expanded to include all types of therapeutic medicines, including insulin, cancer medications, and cardiovascular drugs. Although counterfeit drugs sometimes end up in the pharmaceutical supply chain, the primary source of counterfeit drugs is online pharmacies.²⁴ The National Association of Boards of Pharmacy found that 97% of the Internet pharmacies it examined were not compliant with either federal or state laws, or with industry standards.²⁴

The FDA has the task of making sure that pharmaceuticals are safe and effective, but this task is becoming increasingly difficult, with patients bypassing traditional sources of medication and purchasing them from rogue Internet pharmacies that pose as legitimate businesses.²² Consumers are motivated by lower prices, and some are attracted by the ability to obtain prescription drugs without a prescription.²²

The FDA notes that nearly 1 in 4 Internet users has bought from online pharmacies.²⁵ To educate consumers about the dangers of purchasing prescription drugs online, the FDA has launched a campaign entitled "BeSafeRx: Know Your Online Pharmacy."²⁶

Some Internet pharmacies give the impression that they are located in Canada and are selling legitimate brand-name drugs that have been manufactured in Canada, but many of these legitimacy claims are blatantly false.²² In these cases, the drugs are not approved by the FDA and they are not safe or effective. They are often not even approved by the Canadian government.²⁷ Medicines that are not used in Canada are not subject to the scrutiny of Canada's safety laws.²⁷ Therefore, drugs from Canadian Internet pharmacies can come from anywhere in the world. The fact is that many so-called Canadian Internet pharmacies are not Canadian at all, but are actually based in places such as Belize, Russia, and Vietnam, to name a few.²² A 2005 study found that only 214 of 11,000 online pharmacies claiming to be Canadian were actually registered in Canada.¹⁶ This has made "Canadian" Internet pharmacies the primary supplier of counterfeit drugs to the United States.²⁷

One Canadian online pharmacy has been linked to counterfeit bevacizumab.²⁸ This same online pharmacy blamed the US government for trying to stop its operations, stating on its website, "Washington wants to seize and destroy your safe, affordable imported drugs."²⁷ The

truth is that these drugs are often neither safe nor affordable. As noted before, in most cases, these drugs can harm consumers, because they do not contain the active ingredients to resolve a health issue, and instead they can contain harmful ingredients, such as bacteria and toxins. Of note, in the case of lifestyle drugs, such as sildenafil, the counterfeits often contain some of the active ingredient,²⁹ because the effect of the drug is obvious.

Although Internet pharmacies often boast that they can save consumers up to 75% of the drug cost,³⁰ patients often receive a medication that offers them zero benefits and may cause them more harm than good. Tap water or bacteria at a discount of 75% off the price of the legitimate drug is no bargain for anyone. Although it is possible to obtain legitimate drugs from overseas at considerable discounts,³⁰ the Federal Food, Drug, and Cosmetic Act makes it technically illegal to import prescription drugs into the United States.³¹

Moreover, some of these Internet sites are linked to terrorist groups, such as Hezbollah and Al Qaeda, and others are linked to organized crime—posing a threat to national and international security.¹¹ In an attempt by these sites to make even more profit, consumers may face other consequences of an online drug purchase, including credit card fraud, identity theft, and computer viruses.³² So, what is the real price of an online prescription? *Caveat emptor*—let the buyer beware.

One hopeful sign is that of increased international cooperation. In June 2013, the United States, along with almost 100 other countries, collaborated in the Operation Pangea VI—a global action against online trading of counterfeit and illegal drugs. The FDA reported that the operation eliminated 1677 websites involved with the sale of illegal prescription drugs and seized \$41 million worth of dangerous drugs.³²

The Bevacizumab (Avastin) Case

As noted before, the importation of non-FDA-approved drugs into the United States is illegal. Drugs that are not approved by the FDA or do not contain FDA-approved labeling are considered to be illegal for sale in the United States. Counterfeit cancer drugs first appeared in the United States in February 2012 and 2 subsequent cases were reported in June 2012 and February 2013.³³ All 3 cases concern counterfeits of the cancer drug bevacizumab and were supplied to patients in the United States.³³ According to the FDA, there are only 4 approved suppliers of bevacizumab in the United States. Physicians purchased the counterfeit bevacizumab from unapproved suppliers, at prices below the going price for bevacizumab.³²

Although seeking lower-priced drugs is desirable, prices substantially below customary levels should raise

questions. Thus, physicians need to perform due diligence to make sure that they are buying from legitimate suppliers to avoid putting their patients in harm's way. In 1 case, counterfeit medicines should have been easily detected, because the writing on the box was in French.³⁴

There have been other incidents of physicians supplying patients with drugs from unauthorized suppliers. In 1 case, 7 Ohio oncologists paid \$2.6 million in fines and were sentenced to probation after pleading guilty to a misdemeanor of purchasing unapproved cancer drugs.³⁵ This case also involved Medicare fraud: physicians bought the drugs at a price below the list price but billed Medicare at the list price.³⁵

Incentives and Penalties

According to an article published in the *American Journal of Law & Medicine*, “the success of prescription drugs and their extensive use has attracted unsavory characters interested in exploiting vulnerable patients and the markets for medicines.”¹¹ Although pharmaceutical companies spend considerable amounts of money on the research and development (R&D) of new drugs that benefit society and are approved as safe and effective in the United States by the FDA, suppliers of counterfeit drugs bypass this process and supply these drugs at little cost to them; profit margins are often as high as 3000%.³⁶

One expert estimates that a \$1000 investment in counterfeit prescription drugs can result in a \$30,000 return, which is 10 times the profit rate of trafficking heroin.³⁷ For example, one source reported that selling counterfeit sildenafil “can be as much as 2000 times more profitable” than selling cocaine.³⁸ Also, the risk of being caught is much lower because detection is much more difficult.³⁸

Detection is difficult because medical personnel attribute the problem of drugs that produce poor clinical outcomes to patient variation.¹¹ In most cases, patients are unlikely to suspect that they are using counterfeit drugs. Often, drug packaging is thrown away, which makes it difficult to test for bad drugs, particularly because the drugs may be undetectable in the bloodstream after a few days. As was suggested by 1 case, “the evidence is destroyed the second it is ingested or injected.”¹⁵ Also, patients may not want to reveal that they have bought drugs without a prescription over the Internet. Therefore, the probability of a counterfeiter getting caught can be very low.

The criminal penalties for the sale of counterfeit medications can be far less than the criminal penalties for the sale of illegal narcotics, thus making it more profitable and less risky for criminals to sell counterfeits. It is estimated that counterfeit drugs provide approximately \$75 billion in revenue annually to illegal operators and have caused more than 100,000 deaths worldwide.²⁰ The pen-

alties are obviously too low. The Federal Food, Drug, and Cosmetic Act penalizes drug counterfeiting with a maximum of \$10,000 or 3 years in prison, or both.³⁹ Representative Tim Murphy states, “The penalties for drug-counterfeiting under the Federal Food, Drug, and Cosmetic Act have not been updated since 1938. There is a steeper penalty for counterfeiting a designer purse under the Federal Criminal Code than a drug product under current FDA law.”⁴⁰

By contrast, the penalties for selling narcotics can be life in prison and millions of dollars in fines. One person involved in the bevacizumab case received 6 months of house arrest and 5 years of probation.⁴¹ Clearly, more stringent penalties are needed to discourage counterfeit drug sales. A recent survey by the American Consumer Institute Center for Citizen Research showed that consumers strongly believe that the sale of counterfeit medicines can pose serious health risks to American consumers.⁴² The survey also showed that consumers overwhelmingly support criminal penalties for anyone who knowingly sells counterfeit medicines to Americans online.⁴²

Economic Benefits of Intellectual Property

Innovation is important to economic growth and US competitiveness in the global marketplace. Intellectual property protections provide the ability for society to prosper from innovation. As President Obama has stated, if we are to win the future and to be successful in an increasingly competitive international market, the United States must innovate.⁴³ Innovations create jobs and provide products that enrich consumers’ lives.

In 2010, intellectual property-intensive industries accounted for 27.7% of all US employment.⁴⁴ Such industries paid a 42%-wage premium compared with other industries, and they accounted for 60.7% of US merchandise exports in that year. As the US Department of Commerce puts it, “innovation protected by intellectual property rights is key to creating new jobs and growing exports.”⁴⁵ Alternatively, intellectual property theft reduces incentives to create and innovate, and that, in turn, reduces economic output and employment.

Especially important in terms of innovation are the pharmaceutical and biopharmaceutical industries. These industries typically spend an average of 15% to 17% of their revenues on R&D, which is among the highest rates of R&D spending of any industry. For example, in 2006, the US pharmaceutical industry spent 22% of sales on R&D, whereas all manufacturing spent only 3.3% of their sales.⁴⁵ Counterfeit drugs reduce the incentive to engage in R&D. Indeed, the National Association of Boards of Pharmacy estimated that counterfeit drugs generated \$75 billion in revenues in 2010.⁴⁶ This represents a substantial percentage of lost revenues to the

pharmaceutical industry. However, the attraction of counterfeits is their low prices, and the loss to the industry is presumably less than the estimated sales of the counterfeit drugs, because some consumers would likely not have purchased the drugs at the standard price. Nevertheless, the loss is significant and imposes a cost to society in the form of reduced incentives for innovation.

An example of the loss from counterfeit drugs comes from the experience of Pfizer. In 2010, authorities in 53 countries confiscated 8.4 million tablets, capsules, and vials of counterfeit Pfizer products.⁴⁶ This part of the cost of fighting counterfeit drugs is borne by the companies. Brian Donnelly, PhD, Director of Pfizer’s global security team (the unit that battles counterfeiters) is a pharmacologist who had worked as an FBI special agent for 21 years and is now leading the work on counterfeit drugs.⁴⁶ Resources that could be used for more productive ventures are instead used to deal with the problem of counterfeit or adulterated goods. Such security officers investigate, and then seek cooperation, from public authorities to make arrests.

Implications

Call for Action to Policymakers

The prevalence of counterfeit drugs is increasing, especially with the expansion of the Internet. It is estimated that 36 million Americans have bought drugs online without a valid prescription.⁴⁷ Counterfeit drugs pose a public health hazard, waste consumer income, and reduce the incentive to engage in R&D. The counterfeit problem is especially acute in less developed countries. Counterfeiting involves both lifestyle and lifesaving drugs. Counterfeiting drugs is extremely profitable, and current penalties are insufficient to deter this practice.

A survey of US consumers showed that there is strong support for criminal penalties to combat counterfeit drugs.⁴⁰ Internet pharmacies are a major source of counterfeits, as consumers search for lower-priced drugs or purchase prescription drugs without a prescription. Shortages of drugs exacerbate the problem by increasing prices and enabling counterfeits to enter the market as providers seek to obtain drugs in short supply. The long supply chain, through which some drugs pass, facilitates the entry of counterfeits. Furthermore, the fact that most active ingredients for drugs come from foreign sources adds to this problem.

The loss of profit on an estimated \$75 billion of counterfeit drug sales is significant.⁴³ To illustrate the point, assuming that only 50% of the sales of drugs would occur at customary prices, and because counterfeits are most prevalent with the more profitable drugs, the annual lost commercial profit could be approximately \$18 billion, which could be used for more productive uses or lower prices.

Table Suggestions on How to Reduce Drug Counterfeiting

- Increase public awareness, especially concerning Internet pharmacies
- Improve management of supply chain
- Apply stiffer fines and jail sentences for convicted sellers of counterfeit drugs
- Increase due diligence by physicians when purchasing drugs and stiffer penalties for those who knowingly provide counterfeit drugs to their patients
- Improve controls of secondary drug markets
- Improve cooperation with foreign governments regarding counterfeiting drugs
- Improve quality control by drug manufacturers to avoid drug shortages
- Encourage more voluntary cooperation from companies along the Internet chain, such as credit card companies, domain registrars, Internet service providers, and couriers
- Improve use of technology to track and trace counterfeiting drugs
- Sell drug supplies only to licensed manufacturers
- Construct Internet search algorithms so that legitimate online pharmacies appear first

Several public policy changes would help to improve the situation. Some of these are listed in the **Table**. Overall, technological approaches should be utilized when appropriate and feasible to help ameliorate the counterfeit problem. Drug manufacturers need to improve the quality of the production process to decrease drug shortages. Higher fines, loss of medical license, and jail time should be implemented for physicians who knowingly give counterfeit drugs to their patients.

Penalties for counterfeiting should be increased. Given the difficulties and low probability of detection, penalties would have to be substantial to deter the practice. A 20-year sentence and a life sentence for anyone selling drugs that lead to death is appropriate. More information concerning the hazards of purchasing from Internet pharmacies should be provided so that consumers can make more informed choices. Tracking of drugs is already being enhanced. Additional technological steps, including the possible insertion of radio chips, should also be considered as a way of tightening the supply chain.

The recently enacted drug security law (2013) is an important step in the right direction.⁴⁸ More effective licensure control of drug wholesalers is also important.

Physicians should purchase drugs from only authorized distributors, which would reduce the ability of counterfeits to enter the market.

Greater international cooperation to confront counterfeiting in countries like China should also be considered.

Internet-access companies should be encouraged to make their algorithms list the approved online pharmacies first. These would be pharmacies that meet the

standards of recognized industry organizations or licensing authorities. More voluntary cooperation from companies along the Internet chain, such as credit card companies, domain registrars, Internet service providers, and couriers would make counterfeiting less profitable.

Consumer Education Needed

Consumers should be encouraged to know where the online pharmacy is actually located, and the actual source of their drug supply. In addition to scrutinizing the location of an online pharmacy, consumers should also be leery of any company that will distribute prescription drugs without a prescription. Consumers should also be informed about the extent of counterfeit drugs and the harm they cause. Finally, consumers should be encouraged not to buy prescription drugs without a valid prescription.

When it comes to buying drugs from online pharmacies, consumers should heed the old Latin phrase, *caveat emptor*—let the buyer beware.

Conclusion

Solving the counterfeit drugs problem is important to ensure that patients do not lose faith in the benefits of pharmaceuticals and become nonadherent with their treatments. The expansion of the Internet, and the difficulty in controlling drug suppliers from the Internet, have greatly increased consumer purchases of counterfeit drugs. Controlling the availability of counterfeit drugs is not easy, but it is necessary, given the tremendous public health issues concerning counterfeit drugs, which can harm or kill people. Cooperation is necessary among all the stakeholders involved. ■

Author Disclosure Statement

Dr Blackstone and Mr Pociask reported no conflicts of interest; Dr Fuhr was a member of the multistakeholder roundtable for NeoTract.

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STAKEHOLDER PERSPECTIVE

The Hidden Market of Counterfeit Drugs a Concern for All Stakeholders

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PAYERS: The issue of counterfeit drugs discussed by Blackstone and colleagues is largely unnoticed by the typical health plan in the United States. Health plans pay pharmacies for prescription drugs through pharmacy claims via a pharmacy benefit manager, and they pay physicians and other providers for drugs in the medical benefit through a variety of medical claims systems. In either case, the claim requires that a code that identifies a particular drug be submitted to the plan. The problem is, however, that the code would be the same for a legitimate or a counterfeit agent. The burden of determining whether a drug is counterfeit lies with the ultimate dispenser of the drug to a patient.

Health plans credential physicians before adding them to their networks, and they work with pharmacy benefit managers to ensure that the pharmacy network is of the highest quality, by denying access to or removing from the network pharmacies that have demonstrated fraudulent or unethical behavior in the dispensing of pharmaceuticals.

A bigger issue for health plans is the potential negative effects from patients obtaining and using counterfeit medications without getting the clinical benefit of the drugs. The risks for disease progression, side effects, or the need to change the treatment approach because of a poor response all present issues for the health plan, and can lead to poor patient outcomes and increased costs.

PATIENTS: An educational approach would be an effective way for health plans to communicate to patients regarding the risks of counterfeit medications. Patients need to be educated on the potential risks of using Internet pharmacies to obtain prescription drugs. Health plans usually have a preferred mail order pharmacy in their network, and ordering prescriptions on the Internet is generally allowed for that particular pharmacy. Patients can feel confident that the mail/Internet pharmacy has been chosen based on a number of key criteria, including that they are qualified to meet the needs of the

health plan members, and that the patients need not be concerned about the legitimacy or safety of the medications obtained from this preferred provider.

PROVIDERS: When patients are concerned about the out-of-pocket costs of pharmaceuticals, providers and health plans need to be aware of the risk associated with the use of a secondary market to obtain their medications in an effort to save money. Providers can make patients aware of patient assistance programs or copay coupons that may defer some of the costs of prescription drugs. A majority of patients in a health plan have drug coverage, and physicians have many drugs to choose from with reasonable out-of-pocket costs for their patients. Physicians need to be aware of patients who do not have drug coverage and who may be looking for lower-cost pharmacy options.

POLICYMAKERS/OTHER STAKEHOLDERS: It is clear that the US Food and Drug Administration must work with drug purchasers to establish track and trace capabilities for the drugs in the distribution channels; however, if patients choose an Internet pharmacy, the track and trace system may not be of any benefit. Physicians and pharmacists need to apply common sense and sound business practices when purchasing medications and acknowledge that any discounts will usually come directly from the drug manufacturers and not from a secondary wholesaler, unless there is something potentially wrong with the medication.

At the end of the day, all healthcare providers need to help educate patients on the dangers of ordering medications over the Internet, and especially ordering drugs without a valid prescription. In particular, if drugs are in short supply, the potential for counterfeit drugs increases, and all purchasers and policymakers need to be aware of the risk of fraud when drug supply is a problem.

Blackstone and colleagues are absolutely correct in their warning to patients regarding the purchase of drugs online: *caveat emptor*—let the buyer beware. ■