Prescription Stimulant Sales on the Internet

Anecdotal reports and preliminary studies suggest Internet pharmacies are a significant source of prescription medications, including controlled drugs, obtained for use and misuse in the United States. While many Internet pharmacies are legitimate businesses offering safe and convenient services similar to those provided by traditional neighborhood pharmacies, others — often described as "rogue" operations — engage in practices that clearly are illegal, such as selling unapproved or counterfeit drugs or dispensing drugs without a prescription. Still others exploit loopholes in current US law to engage in "grey area" tactics, such as hiring physicians or others to write "prescriptions" based on a patient-supplied questionnaire, without any direct contact with the patient.

Operators of such sites capitalize on the relatively unregulated and borderless nature of cyberspace. Many of these Internet pharmacies originate overseas.

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operating almost completely outside the purview of US authorities.

The volume of Internet drug sales is not known. However, federal authorities have estimated that 20 million packages containing pharmaceuticals purchased online enter the US each year. One mail processing facility in Miami, FL, handled as many as 150,000 such packages each week. In a joint operation conducted by the US Customs Service and the Food and Drug Administration, agents seized a random sample of drug packages that arrived at international mail centers in seven US cities and two commercial courier facilities. More than 80% of the parcels contained drug products that violated FDA regulations in some way: they were unapproved foreign drugs, controlled substances, or counterfeits. Of the samples subjected to laboratory analysis, 14% contained no active ingredient at all.

Contrary to popular belief, it is illegal to import prescription drugs for personal use except in very limited circumstances. The US Customs Service has the authority to seize any controlled substances on entry. Because of the sheer volume of drugs involved, however, many pharmaceuticals, including prescription stimulants, reach their purchasers unchecked.

Such unregulated access to potent drugs is a new and relatively undocumented phenomenon. Internet sites are easily established, operated, and relocated. Sites owned or hosted outside the US present jurisdictional complications for regulators and law enforcement officials. The use of online pseudonyms, chat rooms, instant messaging, bulletin boards, newsgroups, money wiring services, electronic encryption, and public Internet access, including Internet cafes, enable buyers and sellers to do business over the Internet without making direct contact or creating an identifiable trail.

In recognition of the problem, the Office of National Drug Control Policy has called attention to Internet pharmacies as sources of drugs dispensed outside medical channels and, too often, outside the law.

**SCOPE OF THE PROBLEM**

A number of studies have attempted to assess the role of Internet pharmacies as sources of diverted or abused prescription drugs, but the available data are suggestive or incomplete. For example, a report in the *Journal of the American Medical Association* described a study in which investigators used a popular online search engine to locate 100 Internet pharmacies that offered to sell opiate-containing medications without a prescription — a clear violation of the US Controlled Substances Act (CSA). Of the 100 Internet pharmacies contacted, 35 offered to sell other controlled drugs as well, including benzodiazepines, barbiturates, stimulants, flunitrazepam ( Rohypnol), and gamma hydroxybutyrate (GHB). Twenty-three of the 100 sites were registered to owners outside the US.

Each of these sites required only a shipping address and payment method to complete a drug sale. Complimentary trial offers were featured by one site, and many others boasted of secretive shipping practices to avoid confiscation by government officials. One site advertised, "No labels indicating either package contents or our company name are displayed. And to ensure maximum success in delivery rate, we change the return address for each shipment." It added a "Confiscation Guarantee: we guarantee to reship your order for free in the event of confiscation."

Similar results were reported in a White Paper on Internet Pharmacy issued by The National Center on Addiction and Substance Abuse (CASA) at Columbia University. During a 1-week period, CASA researchers identified 495 Internet sites advertising controlled drugs: 338 "portal sites" that led to another site for purchase of the drugs and 157 "anchor sites" that directly sold the advertised drugs. Drugs advertised included opioids (eg, oxycodone, such as OxyContin; hydrocodone, such as Vicodin; or propoxyphene, such as Darvocet), sedatives (eg, diazepam, alprazolam), and stimulants (eg, dextroamphetamine, such as Dexedrine; methylphenidate, such as Ritalin; or amphetamines).

Forty-seven percent of the sites said the drugs would be shipped from outside the US, 28% said the drugs would be shipped from within the US, and 25% gave no indication of the geographic origin of the drugs. Only 6% of the sites said they required a prescription to complete a sales transaction, and none placed any restriction on the sale of the drugs to children.

In a more exhaustive investigation, the
US Government Accountability Office (GAO; formerly the General Accounting Office) examined the extent to which certain drugs can be purchased over the Internet without a prescription, and whether the drugs shipped are handled properly, approved by the FDA, and authentic. As part of this study, GAO investigators attempted to purchase up to 10 samples of 13 different drugs, each from a different Internet pharmacy site, including sites in the US as well as Canada and other foreign countries. The investigators assessed the condition of the drugs received and forwarded them to their putative US manufacturers to determine whether they were approved by the FDA, safe, and authentic. They also confirmed the locations of several Internet pharmacies and undertook measures to examine the reliability of their business practices.

GAO investigators obtained most of the prescription drugs they sought without providing a prescription, receiving 68 samples of 11 different drugs, each from a different Internet pharmacy site in the US, Canada, or other countries, including Argentina, Costa Rica, Fiji, India, Mexico, Pakistan, Philippines, Spain, Thailand, and Turkey. Five of the US pharmacy sites, and all 18 Canadian pharmacy sites, required a patient-provided prescription, whereas the remaining 24 US sites and all 21 non-Canadian foreign sites provided a prescription based on their own medical questionnaire or had no prescription requirement.

Among the drugs GAO investigators obtained without a prescription were those with special safety restrictions (eg, clozapine, Clozalil) and drugs that are scheduled under the CSA because of their potential for abuse and addiction (eg, oxycodone, hydrocodone). Methylphenidate was not included in this study.

Manufacturer testing found the chemical composition of all but four of the drugs was comparable to the product the GAO ordered. The four aberrant samples were determined to be counterfeit products or otherwise not comparable to the product the GAO ordered. In addition, investigators found questionable entities located at the return addresses on the packaging of several samples, such as private residences. Fourteen of the 68 Internet pharmacy sites from which the GAO obtained samples were found to be under investigation by regulatory agencies for causes that included selling counterfeit drugs and providing prescription drugs where no valid doctor–patient relationship existed. Nine of these were US sites, one was a Canadian site, and four were located in other foreign countries.

The Federal Trade Commission (FTC) also has investigated Internet pharmacy sales. The director of the FTC’s Bureau of Consumer Protection told a Congressional subcommittee:

"Significant potential for injury exists when prescriptions are issued without adequate review of the consumer’s medical history or when unapproved drugs are sold to consumers over the Internet by overseas pharmacies. The Commission has limited anecdotal evidence of specific occasions where consumers have, in fact, received a prescription drug via the Internet that would be clearly inappropriate or even dangerous because of the age, health, or other drug use of the consumer." 10

The FTC’s monitoring activities have led to a few preliminary investigations. In one situation, FTC staff completed two mock online consultations to obtain the prescription drug sildenafil (Viagra). For one of these consultations, the staff member described a number of factors in the “patient’s” medical history that should have raised serious concerns about the appropriateness of issuing a prescription for sildenafil, such as bypass surgery, obesity, family history of heart disease, and the absence of any information about other medications. In both cases, a prescription was issued without question, and the staff member was able to purchase the sildenafil online. The investigation led to referrals to the relevant state medical and pharmacy boards.

In a study that specifically examined availability of methylphenidate and similar drugs through Internet pharmacies, the Prescription Drug Research Center (PDRC) used two different approaches. In the first part of the study, PDRC investigators followed up more than 100 unsolicited offers of drugs in e-mail messages (“spam”) received between November 15, 2003, and January 6, 2004. The surveillance sample is not a true random sample of the universe of Internet pharmacies; in fact, the pharmacies that engage in illicit activities probably were over-represented because of the aggressiveness of their marketing tactics.

None of the Internet sites offered methylphenidate, although several implied that they could provide the drug. Most were portal sites that directed purchasers to one of four or five anchor Internet pharmacy sites. It was not unusual to receive three or more offers a day from different addresses for the same Internet pharmacy. The remainder were either resellers that identified other than a primary Internet pharmacy or that gave no information on pharmacy affiliation.

In the second part of the study, an Internet search was conducted using two major online search engines. The objective was to find Web sites that offered methylphenidate-type products for sale. Specific brand names searched included Concerta, Focalin, Metadate, Methylin, and Ritalin; generic methylphenidate also was searched.

During the web searches, the search engines displayed links to sponsored sites, which advertised products that were the objects of the search. Where the sponsored sites were Internet pharmacies, they were included in the sample. By virtue of the search methods, the Internet pharmacies included in the surveillance sample probably are not representative of all Internet pharmacies.
A total of 100 Internet pharmacy sites were reviewed, as well as an additional 22 sites through which the searcher was forwarded to one of the original 100. Fifteen of the 100 sites (but none of the sites based in Canada) offered methylphenidate products, and all 15 advertised the Ritalin brand product. However, because no products were purchased, it was not possible to verify that the products shipped actually were the products advertised.

Prices advertised by the sites:
- Concerta: $2.58 to $2.86 per 18 mg tablet, with one site offering 36 mg tablets at $6.38 each.
- Focalin: $0.49 to $0.59 per 2.5 mg tablet.
- Metadate: $1.04 to $1.23 per 10 mg tablet.
- Methylin: $0.92 to $1.13 per 20 mg tablet.
- Methylphenidate (generic): $0.36 to $0.43 per 10 mg tablet.
- Ritalin: $0.73 to $0.83 per 10 mg tablet.

Further, some of the sites advertised that no physician’s prescription was required and that the purchaser could make a “consultation” telephone call or complete and return a form in lieu of a physician’s prescription. All of these activities violate federal law.

**Clinical Implications**

Federal regulators have expressed increasing concern about the safety of prescription drugs purchased on the Internet. Specifically, the FDA is concerned about the safety of such medications because of concerns about the lack of adequate physician supervision for consumers who purchase prescription drugs online; the possibility that such drugs may be handled, dispensed, packaged, or shipped incorrectly; and the risk that such drugs may be tampered with or counterfeited.

Until recently, drug counterfeiting in the United States was described by FDA officials as “relatively rare” and “not widespread.” However, the same officials also have acknowledged that the FDA is seeing an increase in counterfeiting activities worldwide, as well as the emergence of more sophisticated ways to introduce fake products into the US drug distribution system. In fact, FDA officials have characterized counterfeiting of pharmaceuticals outside the US as “rampant,” estimating that about 40% of prescription drugs in Argentina, Columbia, and Mexico are counterfeit, as are about half of certain drugs in China.

For example, an FDA analysis of three commonly prescribed drugs purchased from an Internet pharmacy that advertised “Canadian generics” found that the drugs were fake, substandard, and potentially dangerous. For the analysis, FDA investigators purchased three commonly prescribed drugs from a site that had been sending “spam” e-mails promoting its products. The drugs themselves were advertised as generic versions of brand-name medications Viagra (sildenafil), Lipitor (atorvastatin), and Ambien (zolpidem). Because none of the three products had a US-approved generic version at the time, all the advertised drugs were unapproved.

Zolpidem, a Schedule IV controlled substance, is approved in the US for the short-term treatment of insomnia. The product the FDA obtained contained too much active ingredient, including one tablet that was nearly double the labeled potency. Such a “superpotent” product places patients — especially elderly or debilitated patients — at risk for central nervous system depression, which could be fatal.

The so-called “generic” Lipitor (atorvastatin) was found to be subpotent and failed standard dissolution tests, providing an average of 57% of the active ingredient claimed on the label. It also failed FDA’s purity test. Clinically, a subpotent product could present a long-term risk for the complications of high cholesterol, such as heart disease. In addition, the product was furnished to FDA’s online purchaser even though the purchaser reported that he was taking the antibiotic erythromycin, which is contraindicated with atorvastatin.

Sildenafil is sold in the US to treat impotence. The version of this product obtained by the FDA contained too little of the active ingredient, failed the dissolution test, and had an unacceptable level of impurities. Although subpotent sildenafil may not place patients at additional risk, the purchaser informed the firm in its online questionnaire that he was taking erythromycin, which is contraindicated with sildenafil.

Taken together, these examples illustrate the types of clinical dilemmas such
Internet purchases present to physicians, who have no way to know what drugs their patients are using, and whether in fact the substances patients report taking actually are the substances ingested.

**Legal Implications**

Current regulation of Internet pharmacies consists of a patchwork of federal and state laws in a variety of areas. At the federal level, the FDA is granted authority to regulate prescription drugs under the Food, Drug, and Cosmetic Act (FDCA), which governs (among other things) the safety and efficacy of prescription medications, including the approval, manufacturing, and distribution of such drugs (21 USC § 301 et seq). It is the FDCA that requires that prescription drugs may be dispensed only with a valid prescription (21 USC § 353(b)). However, the act does not define what constitutes a valid prescription; rather, each state creates its own definition of a valid prescription under its pharmacy laws. Because such definitions differ from state to state, there is no uniform, national definition. Thus, certain activities associated with Internet pharmacies, such as prescribing drugs without performing an in-person examination, may be explicitly illegal in one state but of ambiguous legal status in another.

Some rogue Internet sites operate in a legal gray area by requiring patients to obtain a prescription before a drug is dispensed but allowing such patients to secure a prescription by completing a questionnaire that is reviewed by a clinician who never examines or speaks to the patient. While this practice has been deemed unprofessional and unethical by the American Medical Association and the Federation of State Medical Boards, it is not necessarily illegal (21 USC §301 et seq).

To close this loophole, Congress has considered legislation to establish a federal definition of what constitutes a valid prescription. In addition, various Congressional committees have held hearings to discuss other legislative solutions, including the establishment of a single federal standard for prescriptions.

The legal issues are clearer with respect to prescription drugs with abuse potential: shipment of controlled drugs into the US is a clear violation of the CSA. Under the CSA, it is unlawful to import a controlled substance into the country unless the importer is registered with the US Drug Enforcement Administration (DEA) and has obtained DEA approval to engage in such importation; illegal importation of controlled substances is a felony that may result in imprisonment or fines (21 USC § 957, 960). Because the DEA considers anyone who causes controlled substances to be brought into the country to be an importer of controlled substances, an individual or pharmacy that causes controlled substances to be mailed or shipped into the US may violate the law and be subject to criminal penalties (69 FR 38920).

The CSA does provide a limited exception for personal medical use, which allows US residents who travel to foreign countries and non-US residents who travel to the United States to carry controlled substances for their legitimate personal medical use. However, this exception does not permit the shipment of controlled substances into the country for purposes of an individual’s personal medical use (21 USC § 956).

Shippments of prescription drugs also may violate state laws if the originating pharmacy is not licensed in the state where the patient resides, although states often face legal barriers when attempting to exercise jurisdiction over foreign pharmacies (21 USC § 396). Because each state board of pharmacy sets its own policies with regard to both Internet and so-called “brick and mortar” pharmacies, state laws regarding Internet pharmacies differ from state to state. While some state laws specify whether or not prescriptions based on patient questionnaires are valid, other state laws fail to address the issue, thus rendering it difficult for some states to prosecute physicians who prescribe drugs without performing an in-person evaluation.

As with pharmacy practice, the practice of medicine is regulated primarily at the state level by medical boards. According to the Federation of State Medical Boards (FSMB), which coordinates policy among all state medical boards, “[t]he primary responsibility and obligation of a state medical board is to protect consumers of health care through proper licensing and regulation of physicians.”

If a physician violates a state law or regulation, medical boards generally have the authority to discipline the physician through modification, suspension, or revocation of the doctor’s license to practice medicine in that state.

In reality, however, laws regarding medical practice vary widely in strength and effectiveness from state to state. While some states have strong laws that explicitly prohibit activities such as prescribing drugs without conducting an in-person examination, other states have weaker laws, inadequate enforcement resources, or both.

**Policy Implications**

The advent of Internet pharmacies raises new challenges to public agencies and private sector organizations charged with safeguarding and regulating the nation’s supply of prescription drugs. Operators of Internet pharmacies often are located beyond the territorial limits and legal jurisdiction of the US. Others operate within the US, but their use of the Internet enables them to “anonymously reach across state borders to prescribe, sell, and dispense prescription drugs without complying with state requirements.”

Federal and state regulators are struggling to find ways to deal with the presence of Internet pharmacies in gen-
eral and Web sites that illegally sell controlled drugs in particular. State medical and pharmacy boards have expressed concern that their existing enforcement tools are not adequate to police the Internet. In many cases it can be difficult, without extensive investigation, to identify the name, location, and state of licensure or registration for the physicians, pharmacies, and Web site operators involved in Internet operations. For example, regulators in Arizona have struggled to untangle jurisdictional is-

able that some Internet pharmacies have exploited gaps in the current system to prescribe and dispense potentially dangerous quantities of highly addictive prescription drugs. To combat such abuses, legislators and interest groups have proposed an array of solutions, including establishing a federal definition of what constitutes a valid prescription, requiring physicians to conduct in-person examinations, mandating that Internet pharmacies disclose identifying information about themselves and the physicians

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suces and locate Web site proprietors. The Arizona State Attorney General has tried to stop out-of-state and overseas Internet pharmacies from doing business with state residents but concedes that his office lacks the resources to do so.

The DEA also maintains that it is ill equipped to handle the onslaught of cases. Along with US Customs agents, the DEA has authority to seize inbound parcels of foreign pharmaceuticals at the US border. While it is difficult to prosecute the overseas pharmacies from which shipments originate, US buyers can be prosecuted for smuggling illegal drugs into the country. However, DEA representatives acknowledge that they have been slow to fine, jail, or penalize anyone for such violations.

PROPOSED SOLUTIONS

It is clear from the limited data avail-

they employ, giving state prosecutors the authority to seek nationwide injunctions against rogue sites, educating consumers about the potential dangers of buying drugs online, and establishing certification programs to identify legitimate Internet pharmacies.

An FTC review of almost 100 Internet pharmacy sites found that very few provided adequate identifying information. Even when the parties could be located, it proved difficult and costly for state medical or pharmacy boards to pursue enforcement actions against an out-of-state physician or pharmacy prescribing or dispensing prescription drugs inappropriately via the Internet.

To address this problem, the FDA, the GAO, and several members of Congress have urged that online pharmacies be required to disclose their owners, locations, prescribing professionals, affiliated

“brick and mortar” pharmacies, and telephone numbers. House Resolution 3880, which incorporates most of these requirements, was the subject of hearings in the House Government Reform Committee. The measure has been endorsed by the principal organizations representing medicine, pharmacy, and their regulatory boards, as well as by the Attorney General of the State of Virginia.

Congress also is exploring the possibility of controlling the means by which rogue Internet sites do business by restricting their ability to advertise on search engines, make credit card sales, and ship prescription drugs to consumers. Two major Internet search engine providers, Yahoo! and Google, have changed their policies and now say they accept advertising only from Internet pharmacies that have been accredited by a third-party verification system called SquareTrade. Federal Express, United Parcel Service, and Visa routinely assist the DEA in investigating and prosecuting rogue online pharmacies. Because federal and state regulators face many legal barriers when attempting to exercise jurisdiction over rogue pharmacies based in foreign countries, placing limits on the degree to which search engines, credit card companies, and shipping entities facilitate prescription drug purchases from rogue sites may be one of the only ways to control illicit sales by foreign online pharmacies.

Since 1999, the FDA, DEA, and US Customs Service increasingly have worked together to intercept parcels containing illegal prescription drugs. The FDA has created an internal task force that is exploring methods of strengthening the pharmaceutical distribution system, blocking illegal products from crossing US borders, and quickly alerting consumers and health care professionals when counterfeit products are identified. The FDA also routinely works with the DEA to find and punish rogue pharmacy site operators. The DEA has
greater authority than the FDA to prosecute criminals overseas but still must rely heavily on foreign law enforcement and Internet service providers to do so. In its 2004 National Drug Control Strategy, the administration announced that the DEA will deploy sophisticated web crawler and data mining technology to generate investigative leads for enforcement agencies.5

Private-sector organizations have begun to promote uniform standards. For example, NABP has established the Certified Internet Pharmacy Practice Sites (VIPPS) program, a certification program that "identifies to the public those online pharmacy practice sites that are appropriately licensed, are legitimately operating via the Internet, and that have successfully completed a rigorous criteria review and inspection."20 According to NABP, the VIPPS program was developed in order to improve the safety of online pharmacy practices and to "provide a means for the public to distinguish between legitimate and illegitimate online pharmacy practice sites."25

Canadian pharmacies may be certified under the VIPPS program, but only if they do not export drugs to the US.29 However, NABP has indicated that it may extend its VIPPS certification program to Canadian pharmacies that sell to US consumers if Congress approves drug importation or if the US Department of Health and Human Services "does not stop the state and local governments that already are re-importing drugs."30

Like NABP, the FSMB has developed a specific policy with regard to online pharmacies and doctors that prescribe drugs over the Internet. According to FSMB’s model guidelines on the subject, electronic technology "should supplement and enhance, but not replace, crucial interpersonal interactions that create the very basis of the physician–patient relationship."21 To that end, FSMB guidelines declare that physicians who use the Internet as part of their medical practice should conduct a physical evaluation of the patient before providing treatment. The guidelines emphasize that "[t]reatment, including issuing a prescription, based solely on an online questionnaire or consultation does not constitute an acceptable standard of care."31 FSMB officials argue that physicians who prescribe on the Internet should be licensed in all states in which their patients reside,21 a practice that would subject them to scrutiny by the medical boards in each of those states.

Similarly, the American Medical Association (AMA) has established detailed policies regarding the safe practice of online medicine.3 The AMA guidelines, like those promulgated by FSMB, make it clear that a physician should perform a physical evaluation of the patient before prescribing any medication, and advise against prescribing drugs to patients solely on the basis of online communications such as questionnaires. The AMA guidelines also call for physicians to be licensed in every state in which their patients reside. However, such professional standards are not enforceable legally in the absence of state laws codifying the requirements.

NEXT STEPS

Given their role in the importation of counterfeit drugs and the diversion of drugs with abuse potential, including methylenidate and other central nervous system stimulants, the enhanced regulation and oversight of Internet pharmacies is needed urgently. A useful first step would be for the US to enact legislation that closes loopholes in current law that are being exploited by unethical operators. Possible legislation could include the definition of a legal prescription or the requirement for identification of Internet pharmacy owners and prescribers.

An essential next step is to increase knowledge of the drugs obtained through Internet pharmacies, who purchases them, and the extent to which they are purchased for other than medical use. Of the relatively few published studies,8,11,14,32 most either have not specifically examined purchases of controlled drugs or have not included prescription stimulants such as methylenidate. Even so, what we know of current patterns of methylenidate abuse (ie, for so-called "performance enhancement") and the populations most likely to be involved (high school and college students and other young adults) suggests that Internet pharmacies would be a more accessible and appealing source of the drugs than, for example, a street drug dealer.

REFERENCES


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