



# Counterfeiting, Compliance, and Controls

Jill Wechsler

FDA and manufacturers seek to curb drug counterfeiting while legislators consider liberalizing drug importing policies to cut pharmaceutical costs.

**A** surge in imports of prescription drugs into the United States is raising concern at FDA and among manufacturers about opening the door to a flood of counterfeit and unapproved medicines. Export officials estimate that 20 million packages containing pharmaceutical products come into the United States each year and that 14% have something wrong with them. An increase in the number of Internet pharmacies is spurring the trend as well as higher drug prices in the United States compared with other nations. FDA recently announced increased efforts to detect and block sales of bogus drugs, while manufacturers are doing more to track and publicize the dangers of such products.

Ironically, Members of Congress are pressing for legislation that would make it easier for individuals and pharmacists to reimport low-cost drugs from abroad. Advocates aim to increase consumer access to less-expensive medicines, despite FDA and industry claims that the policy is unwise and unworkable. Manufacturers are examining how new technologies may help prevent product tampering and identify counterfeits and are backing policies to protect product names and patient safety—and high revenues.

## Attack on counterfeits

As counterfeit cases piled up in recent months, FDA launched a more aggressive program to halt the influx of bogus drugs from abroad. The agency established an internal task force in July 2003 to explore the use of new technologies and to identify enforcement actions that could stymie the distribution of counterfeit medical products. The panel, which is led by John Taylor, associate commissioner for regulatory affairs, and Bill Hubbard, associate commissioner for policy & planning, is scheduled to report recommendations this month.

The initiative stems from evidence of the rising distribution of counterfeit finished pharmaceuticals in the United States, which is more alarming than the sales of phony bulk drug ingredients that were more common. One report speculates that some low-cost or free drugs intended for foreign medical aid programs are being diverted by unscrupulous distributors. FDA also points to

a rise in smaller secondary wholesalers and distributors that create more opportunities to introduce unregulated products that appear legitimate into the US market.

FDA opened 22 counterfeit drug cases in 2002 and 20 cases in 2001—a big jump from approximately five or six cases each year previously. Since 1996, FDA investigations of counterfeiting cases have led to 44 arrests and 27 convictions. Most cases have involved high-volume drugs such as statins, AIDS therapies, and antidepressants. FDA has found counterfeit medicines with inactive, subpotent, or superpotent ingredients or impurities that could harm patients. Some counterfeit versions of Procrit (epoetin) contained nonsterile tap water that can cause blood stream infections. In 2002, counterfeiters substituted insulin for Eli Lilly's (Indianapolis, IN) injectable drug Zyprexa (olanzapine). A counterfeit version of Serono's (Rockland, MA) AIDS treatment Serostim (somatropin) had no active ingredient at all. Pfizer (New York, NY) recently warned pharmacists of a widespread distribution of unauthorized Lipitor (atorvastatin calcium) tablets that patients found to have a bitter taste.

The Prescription Drug Marketing Act (PDMA) of 1988 provides FDA with the authority to track illegal drug distribution in the United States. PDMA requires wholesalers to keep paper records of a drug's source and distribution history to provide a pedigree for prescription products. However, the tracking requirements are expensive, and FDA has failed to finalize PDMA's implementing regulations because of objections from wholesalers. The current surge in the sale of counterfeit products is putting pressure on FDA to implement the tracking program. At the same time, PDMA appears increasingly outdated because it fails to reflect the emergence of more-secure and more-efficient electronic authentication technologies. One issue that is under review is whether Congress should revise PDMA to boost FDA enforcement options and to update tracking procedures.

Meanwhile, FDA has faced criticism from Congress about lax agency enforcement in the import area. In June 2003, the House Energy and Com-

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merce Oversight Subcommittee held a hearing to examine a major mix-up that allowed a large supply of unapproved Viagra to leave the Miami Import Office (Miami, FL) where it was being detained. FDA officials said that they were investigating and addressing irregularities in the Miami operation but acknowledged that a lack of resources and the need to address other important issues such as homeland security and bovine spongiform encephalopathy (BSE) have prevented more attention to import issues. Members of the House panel expressed dismay and called for immediate attention to illegal imports and counterfeits.

### New deterrents

Whether FDA needs expanded legal authority to prosecute and levy stiffer penalties on counterfeiters is one issue to be addressed by FDA's counterfeit drug task force. The panel also seeks to identify new technologies that can ensure product and package integrity and improve tracking. Most anticounterfeit efforts involve iden-

### FDA—a strict enforcer

FDA's anticounterfeiting initiative fits agency efforts to heighten its profile as a strict enforcer of regulatory policies. In recent months, some members of Congress and patient advocates have complained that FDA was issuing fewer warning letters as part of a more lax oversight approach. The critics pointed specifically to delays in challenging misleading drug advertising and promotional activities because of the agency's pro-industry stance.

In response, FDA Commissioner Mark McClellan issued a white paper on 30 June 2003 highlighting the agency's efforts to boost enforcement actions ("Protecting the Public Health: FDA Pursues an Aggressive Enforcement Strategy," [www.fda.gov/oc/whitepapers/enforce.html](http://www.fda.gov/oc/whitepapers/enforce.html)). The document cites evidence of "dramatically increased enforcement" that is particularly related to pursuing criminal charges against parties involved in activities that could pose serious threats to public health. In 2002, FDA initiated 15 injunctions (up from 11 in 1998), 5025 recalls (versus 3532 in 1998), 286 arrests, and 317 convictions.

FDA points to unprecedented success during the past three years in collecting record-breaking penalties from medical product manufacturers,

including

- TAP Pharmaceuticals (\$879 million settlement for violations of PDMA)
- Schering Plough (\$500 million for failure to comply with good manufacturing practices)
- AstraZeneca (\$355 million for healthcare fraud)
- Guidant (\$92.4 million for failure to report medical-device malfunctions)
- Aventis (\$33 million for submitting false information to FDA)
- Wyeth Ayerst (\$30 million for good manufacturing practices noncompliance).

The white paper also notes that FDA is stepping up actions to prevent manufacturers from engaging in inappropriate promotional practices. So far this year, FDA has issued a dozen letters warning companies about misleading advertising and marketing activities, many of which require corrective actions. FDA critics have complained that new procedures requiring FDA's chief counsel to review all warning letters before they are sent out has stymied timely agency action against unbalanced direct-to-consumer advertising. In recent months, FDA officials have responded with procedural changes to speed up the letter review and oversight process.

tifying look-alike packaging that can be very similar to the original and can fool health professionals as well as consumers. However, because phony drugs can be put in highly authentic-looking packages, manufacturers and regulators are examining ways to incorporate authentication substances (i.e., chemical taggants) into the drug product itself. Counterfeit experts are examining whether such tech-

nologies are cost-effective and practical to implement.

In addition, FDA is reviewing several strategies for countering illegal imports, including

- boosting border controls. FDA is working with US Customs and Border Protection to examine which counterfeits are arriving from foreign countries. These agencies are conducting blitz op-

erations at several international mail facilities.

- expanding federal-state initiatives. FDA is collaborating with states such as Florida, which has adopted stronger drug wholesaler licensing requirements that may provide a model approach for other states. Florida has indicted several people for marketing adulterated medicines such as diluted Epogen and illegal Viagra.
- strengthening the drug distribution system. FDA may encourage wholesalers to adopt a code of conduct, possibly in coordination with the National Association of Boards of Pharmacy.

## Industry action

FDA's counterfeiting task force will gain assistance from a private sector expert working group that has been examining anticounterfeiting issues for more than a year. The working group also is finalizing a report on technologies to better secure the drug distribution chain. The report includes information about anti-tampering efforts and the detection of bogus products.

To spur FDA enforcement efforts now, manufacturers and wholesalers recently agreed to inform the agency more quickly about evidence of new counterfeit products. Members of Pharmaceutical Research & Manufacturers of America (PhRMA) and the Healthcare Distribution Management Association (HDMA) now notify FDA's Office of Criminal Investigations (OCI) about suspected counterfeit drugs within five days of discovering the evidence. FDA may or may not release the information, depending on the potential risk to patients and the need for confidentiality to track the culprits.

PhRMA's broader anticounterfeiting program, which the organization announced in June 2003, also calls for an industry-government summit meeting to examine the need for additional legal authority to curb the influx of counterfeit medicines. Another reason for manufacturers to battle illegal knock-offs is to protect against liability claims. According to *The Economist* (1), Serono settled a lawsuit from a group of US patients claiming that the company should have taken more precautions to prevent counterfeit Seros-tim from entering the distribution chain.

In addition to battling more counterfeits at home, FDA officials are working with manufacturers and foreign governments to stem widespread bogus drug marketing in both developing and developed countries. FDA notes that Chinese counterfeiting of some drugs may be as high as 50%, and estimates are about 40% for fake pharmaceuticals in Argentina, Colombia, and Mexico.

Counterfeiting is a significant problem for pharma manufacturers in Russia also. With approximately 2500 distributors, the Russian pharmaceutical market is very complex and regulatory processes are in a state of flux. Recent tax increases on legal imports and a new pharmaceutical certification system add to the cost of marketing legitimate products, which further encourages counterfeiting. A survey that was sponsored by Russia's Association of International Pharmaceutical Manufacturers (AIPM) and the Coalition for Intellectual Property Rights (CIPR) in 2002 found that counterfeits account for 12% of the total Russian pharmaceutical

marketplace—a much higher figure than earlier government estimates of 3–7%. This development now costs pharmaceutical manufacturers more than \$250 million each year in lost sales and increased enforcement expenses. AIPM Executive Director Robert Rosen says that drug counterfeiting has not yet hit epidemic proportions but is growing exponentially. Pharma company executives consider counterfeits and look-alike products a top challenge and seek tougher Russian government enforcement of intellectual property laws and stiffer penalties for counterfeiting.

### Reimport debacle

However, industry critics in the United States claim that drug counterfeiting is on the rise because legitimate pharmaceuticals are too expensive. In July 2003 a group of legislators orchestrated and won a high-profile battle to permit the reimport of low-cost drugs from other countries. Current law permits only licensed manufacturers to reimport FDA-approved products from abroad, but Congress has been pressing

### Senate backs pediatric drug testing

Before leaving Washington for its August 2003 recess, the Senate approved legislation authorizing FDA to require pharmaceutical companies to test new drugs in children. The Bush administration and manufacturers supported the bill (S. 650), which clarifies the legality of FDA's pediatric rule. The rule, which requires manufacturers to conduct pediatric safety and efficacy tests on new drugs that are prescribed for children, was struck down by a federal court in 2002. Although manufacturers feel that FDA does not need specific authority to require pediatric testing, regulators and the medical community consider it important to have a clear legal basis to back up its voluntary testing incentive program, which extends exclusivity to products that manufacturers test for use in children. The industry succeeded in adding a sunset provision to the legislation, that requires Congress to reauthorize the test requirement policy in 2007 when the pediatric exclusivity program also expires. The House is expected to adopt a similar bill possibly this month.

for a more liberal approach. In 2000, legislators approved a limited expansion in reimporting, provided that FDA can certify that it can ensure the safety and quality of such products. Twice since then,

agency officials have announced their inability to certify the program, pointing to the huge volume of imports that FDA would have to monitor and its lack of resources to do so.

In June 2003, the House and Senate adopted separate Medicare reform bills, each containing a provision to allow reimporting from Canada, with the usual FDA certification caveat. This prompted a coalition of dissatisfied lawmakers to press for

adding a stronger proposal to the final Medicare pharmacy benefit program under negotiation by House and Senate leaders. Just before adjourning for the August 2003 recess, the House approved a bill (HR 2427) requiring FDA to establish a system that allows individuals, pharmacies, and wholesalers to buy pharmaceuticals from a list of 25 developed nations, including Canada, countries that make up the European Union, and Israel. The bill,

sponsored by Rep. Gil Gutknecht (R-Minn), drops the FDA certification requirement and instead calls for imports to be approved by FDA and to be made in facilities that meet FDA manufacturing standards. The bill also requires manufacturers to use counterfeit-proof packaging such as color-coded sealed packages and blister packs to ensure the safety of imported products.

The bill is highly impractical and unlikely to be implemented. One FDA estimate is that such protective technologies could cost manufacturers \$2 billion to adopt. The measure provides no funding for FDA to implement such a program, which would cost at least \$100 million to establish. Congressional Budget Office analysts predict that drug reimporting will not cut costs for Medicare or patients. Also, strong bipartisan opposition exists in the Senate: 53 Senators recently signed a letter backing a proposal that requires FDA to certify the safety of any reimported drugs.

Despite these clear shortcomings, the bill passed the House by a healthy margin (243–186) when a significant group of Republicans joined with most Democrats to overcome strong opposition to the measure from the White House, GOP leaders, and manufacturers. The legislators approved the bill largely to send a loud message to pharma companies to change their current pricing strategies that rely on high US revenues to support worldwide R&D. Heavy-handed lobbying against the bill by manufacturers probably worked against them in the end, as the public responded to industry's willingness to spend enormous time and resources to defeat what many considered a reasonable measure. Even House leaders who opposed the Gutknecht bill acknowledged that if Medicare has to pay billions of dollars for outpatient prescription drugs, then the industry has to offer US patients fairer prices. The Gutknecht bill may be ill-conceived and never become a law, but manufacturers would be wise to consider it as a sign of significant change in the willingness of US consumers and the health-care system to support what appears to be an unfair system.

### References

1. "Imitating Property is Theft," *The Economist*, 52–54 (17 May 2003). **PT**