

Reducing the Threat of Counterfeit and Unapproved Drugs in Clinical Settings

Background

Counterfeit and unapproved drugs pose a serious threat to patients in the United States (U.S.) and abroad. Efforts to combat the use of counterfeit and unapproved drugs have become increasingly challenging, as supply chains have become more complex and global. Foreign sourcing and manufacturing of medical products has increased, and advanced counterfeiting techniques pose new challenges for regulators, providers, payers, and patients. Recent high-profile cases, such as the incident involving the sale of a counterfeit version of the oncology drug, Avastin, indicate that there are significant incentives – including demand, ease, high payoff, and low risk of consequences or penalties – for illegitimate entities to sell unapproved and counterfeit drugs.¹ As such, it appears that the threat from counterfeit drugs continues to grow; according to the European Commission, the number of counterfeit drugs seized by European Union Customs tripled between 2006 and 2009.²

Counterfeit and unapproved drugs pose unique hazards to patients. Unapproved drugs are drug products which are sold without regulatory or market approval from health authorities. These products can include those which are illegally diverted from foreign countries and sold within the U.S. Unapproved drugs may be counterfeit, contaminated, improperly stored and transported, ineffective, and/or unsafe. Unapproved drugs may also lack the required labeling to ensure safe and appropriate use. Recent examples of unapproved drugs include cosmetic injectables sold from foreign and unlicensed suppliers, which were illegally marketed and distributed in the U.S.³

Counterfeit drugs falsely represent a product's identity through unauthorized representation of a legitimate trademark, trade name, or other likenesses.⁴ Counterfeiting can apply to both branded and generic products. Counterfeit products may fail to meet the quality and safety standards established by national regulatory authorities, and may contain dangerous substances, incorrect dosages, or no active ingredient. It is common for a counterfeit drug to be substandard, unapproved, or both.

¹ "Counterfeit Doses of Avastin Distributed in the U.S." *The New York Times*, 15 Feb. 2012. Retrieved July 2, 2013, from http://www.nytimes.com/2012/02/15/business/counterfeit-doses-of-avastin-distributed-in-the-us.html?_r=0.

² Q&A: Directive on falsified medicines. European Union. February 16, 2011. Retrieved July 2, 2013, from <http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/11/91>.

³ U.S. Food and Drug Administration. (December 2012). Drug Integrity and Supply Chain Security (page): Letters to Doctors about Risks of Purchasing Unapproved Versions of Botox and Other Medications from Foreign or Unlicensed Suppliers. Retrieved June 26, 2013, from <http://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/ucm330610.htm>

⁴ Government Printing Office. United States Code, 2010 Edition. Title 21 Federal Food, Drug, and Cosmetic Act. Subchapter II – Definitions. Retrieved June 26, 2013, from <http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapII.htm>

Emerging Trends of Counterfeit and Unapproved Drugs

Although data associated with counterfeit and unapproved drugs are limited due to the clandestine nature of counterfeiting, certain trends have emerged which may indicate that a wide spectrum of counterfeit drugs are being manufactured and distributed. While reports of counterfeit and unapproved drugs were initially associated with “lifestyle drugs” (e.g., those for erectile dysfunction, weight loss), counterfeiters have expanded into more profitable and specialty markets, including drugs for chronic and life threatening diseases. Investigations and seizures have revealed counterfeit and unapproved versions of HIV/AIDS drugs, pain drugs, antibiotics, insulin, cholesterol drugs, hormone replacement therapy, flu drugs, cancer drugs, anti-arthritic drugs, cardiac drugs, anti-parasitic drugs, and antihistamines.⁵ Research has indicated that in 2011, cancer drugs represented the eighth most commonly counterfeited medical product worldwide.⁶

Threat of Counterfeit and Unapproved Drugs within Clinical Settings

In recent years, unscrupulous distributors have expanded their tactics to target clinical settings for the sale of counterfeit and unapproved drugs. Medical offices are often contacted through mass advertising campaigns via “blast faxes”, phone calls, direct email, and online marketing. These distributors often target clinics and hospitals for sale of physician-administered drugs, including a variety of injectable drugs.⁷

In 2012, the U.S. Food and Drug Administration (FDA) issued public alerts in several instances warning that unapproved and potentially counterfeit versions of cancer drugs had infiltrated the U.S. supply chain. In one such case, an investigation revealed that counterfeit versions of Avastin, an injectable oncology drug which is administered in clinics, hospitals, and physician’s offices, lacked the active ingredient found in the genuine version.⁸ Counterfeit versions of Altuzan, a product approved for sale within Turkey but unapproved for market within the U.S., similarly contained no active ingredient.⁹ Further investigations have suggested that the unapproved versions of Avastin and Altuzan were routed through numerous countries and secondary distributors, obscuring their location of origin.¹⁰ FDA issued notification letters to medical practices alerting them that they may have received unapproved or counterfeit drug products from a particular unlicensed distributor, and advising of the public health risks.

Health care professionals who purchase and administer counterfeit and unapproved drugs in a clinical setting can face severe penalties. State boards of medicine have taken action against health professionals who have knowingly purchased and administered counterfeit and unapproved drugs. Penalties associated with purchasing and administering counterfeit products can include a suspension of

⁵ Liang, BA. “Fade to Black: Importation and Counterfeit Drugs.” *American Journal of Law & Medicine* 23 (2006): 279-323. Retrieved: <http://anesthesia.ucsd.edu/research/faculty-research/Documents/AJLMFadetoBlack.pdf>

⁶ “Counterfeit Cancer Medications Multiply.” *Wall Street Journal*. N.p., December, 31, 2012. Web. Retrieved June 26, 2013, from: <http://online.wsj.com/article/SB10001424127887323320404578211492452353034.html>

⁷ “How Fake Cancer Drugs Entered the U.S.” *Wall Street Journal*. N.p., July 20, 2012. Web. Retrieved June 26, 2013, from <http://online.wsj.com/article/SB10001424052702303879604577410430607090226.html#project%3DAVASTINTRAIL0712%26articleTabs%3Darticle>

⁸ U.S. Food and Drug Administration. (July 2012). Drug Safety and Availability (page): Counterfeit Version of Avastin in U.S. Distribution. Retrieved June 26, 2013, from: <http://www.fda.gov/drugs/drugsafety/ucm291960.htm>.

⁹ Kuehn, BM. (2013). FDA Warning: New Batch of Fake Bevacizumab Found. *JAMA* 309(9):864. doi:10.1001/jama.2013.1719.

¹⁰ “How Fake Cancer Drugs Entered the U.S.” *Wall Street Journal*. 20N.p., July 20, 2012. Web. Retrieved June 26, 2013, from: <http://online.wsj.com/article/SB10001424052702303879604577410430607090226.html#project%3DAVASTINTRAIL0712%26articleTabs%3Darticle>

medical licensure and medical malpractice suits.^{11,12} Health care professionals who falsely bill public and private payers for reimbursement of counterfeit and unapproved drugs may face prosecution and fines.^{13,14} However, there has been inconsistent and sparse enforcement of professional sanctions against health care professionals who purchase or use counterfeit or unapproved drugs beyond the few cases that are initially investigated and prosecuted by law enforcement agencies.

Efforts to Combat Counterfeit and Unapproved Drugs

Federal agencies have undertaken extensive efforts to combat the manufacture and distribution of counterfeit and unapproved drugs within the U.S. These efforts span inter-agency working groups and cooperative activities, as well as numerous initiatives within individual departments, agencies, and offices.¹⁵

The FDA plays a critical role in the investigation and enforcement of violations involving FDA-regulated products. FDA's Office of Criminal Investigations (OCI) conducts and coordinates criminal investigations regarding the manufacture and sale of counterfeit or unapproved drugs, as well as the illegal diversion of pharmaceuticals and other regulated products. Other agency components, such as FDA's Office of Drug Security, Integrity, and Recalls (ODSIR), works to ensure the quality, integrity, and security of drugs for U.S. patients. Among the activities conducted by the office, ODSIR ensures the integrity of the pharmaceutical supply chain, enforces legal requirements to promote the quality and integrity of imported products, and raises public awareness of drug security threats.¹⁶ In addition, FDA manages a counterfeit alert network to inform health professionals and patient groups about counterfeit drug incidents and measures to take to minimize exposure. FDA's MedWatch Program solicits information from patients and health care professionals regarding potential unapproved or counterfeit products. This voluntary reporting system captures information on suspect counterfeit drugs and other product quality issues from patients, health care professionals, and other stakeholders, in addition to adverse events that patients may experience.

Expansion of the nation's regulatory capacity to combat counterfeit and unapproved drugs and ensure a safe drug supply has also been a legislative priority. In 2012, Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA), which provides FDA additional measures for seizing counterfeit and unapproved drugs, inspecting foreign factories abroad, and protecting the safety and quality of the supply chain.¹⁷ Currently, Congress is considering national "Track and Trace" legislation

¹¹ Wachter, K. "More Counterfeit Bevacizumab Raises Legal Questions for Oncologists." *Oncology Report Digital Network*. N.p., May 1, 2012. Web. Retrieved July 11, 2013, from <http://www.oncologypractice.com/oncologyreport/news/practice-trends/single-article/more-counterfeit-bevacizumab-raises-legal-questions-for-oncologists/8a39735c4abae7419679ae4a20d12bdf.html>

¹² Nevada Medical State Board of Examiners. (November, 2010). Retrieved July 11, 2013, from http://www.medboard.nv.gov/Discipline/Seldon_Stephen.htm

¹³ U.S. Department of Justice (April 2008). Press Release (page): Oncologist and His Wife Agree to Settle Civil Fraud Allegations Involving Importation of Oncology Drugs from Canada. Retrieved from: <http://www.justice.gov/usao/nye/pr/2008/2008apr24.html>

¹⁴ Wall Street Journal, November 20, 2012, "U.S. Fake-Drug Probe Puts Spotlight on Role of Doctors," Retrieved from: <http://online.wsj.com/article/SB10001424127887323353204578129682462065220.html>.

¹⁵ Counterfeit Pharmaceutical Inter-agency Working Group Report to the Vice President of the United States and to Congress. [Washington, D.C.]: Executive Office of the President of the United States, 2011.

¹⁶ U.S. Food and Drug Administration (December 2012). Drug Integrity and Supply Chain Security (page): Office of Drug Security, Integrity, and Recalls. Retrieved June 26, 2013, from <http://www.fda.gov/drugs/drugsafety/drugintegrityandsupplychainsecurity/default.htm>

¹⁷ Steinbrook R, Sharfstein JM. (2012). The FDA Safety and Innovation Act. *JAMA* 308(14):1437-1438. doi:10.1001/jama.2012.12829.

which would aid in securing the movement of drugs through the supply chain by creating a system for tracing products.¹⁸ A more secure supply chain will significantly reduce the prevalence of counterfeit and unapproved products on the U.S. market, but there will remain substantial incentives for the production, sale, and purchase of counterfeit and unapproved products.

Strategies for Reducing Counterfeit and Unapproved Drugs in Clinical Settings

Generally, efforts taken by FDA to combat counterfeit and unapproved products have focused on key players in the drug supply chain, such as drug manufacturers and distributors. While these efforts have helped to ensure the security and integrity of the drug supply chain, gaps remain in the knowledge and enforcement on the “demand side” of counterfeit drug purchasing. The purchase of counterfeit and unapproved drugs by patients and health care professionals has become an increasing problem that is neither well understood, nor within the traditional scope of the FDA’s investigation and enforcement practices. Countering the purchase of counterfeit and unapproved drugs will require substantial commitment and effort across multiple health care stakeholders, including health care professional licensing boards, professional societies, malpractice insurers, and payers. By capitalizing on each stakeholder’s distinct knowledge and regulatory capacities, FDA, in partnership with stakeholders, can further reduce the demand for counterfeit and unapproved drugs.

The Engelberg Center for Health Care Reform at the Brookings Institution is collaborating with FDA’s Office of Drug Security, Integrity, and Recalls to convene an expert workshop exploring strategies for reducing the purchase and distribution of counterfeit drugs, with a particular emphasis on medical professionals within clinical settings. The workshop will delve into how stakeholders can leverage institutional influence or authority to increase awareness and improve compliance and professional behavior. Specific solutions for a range of issues will be addressed, including improved education and engagement of stakeholders within the healthcare delivery system; development and implementation of a more effective reporting system that aggregates and disseminates information on incidents involving counterfeit or unapproved drugs; strategies to incentivize good purchasing practices and reporting of improper conduct; and development of a collaborative framework that facilitates enforcement of deterrents for the purchase of counterfeit and unapproved drugs that involve not only criminal investigation and prosecution, but also potentially the loss of licensure, reimbursement privileges, or malpractice insurance.

Meeting Objective and Discussion Questions

This workshop will explore strategies to address remaining gaps in the knowledge and enforcement of counterfeit and unapproved drugs within clinical settings. During the workshop, focused sessions will examine current approaches to limit the use of counterfeit and unapproved drugs, strategies to improve communication and awareness between stakeholders, and innovative methods for deterring the use of counterfeit drugs and unapproved drugs. Questions relating to those areas have been posed to help guide discussion.

Session I: Current Approaches to Controlling Counterfeit and Unapproved Drugs, and Remaining Gaps in Knowledge and Enforcement

- What efforts have been undertaken to secure the drug supply chain?
- What is the scope of FDA’s ability to ensure drugs are safe, effective, and high quality?

¹⁸ Government Printing Office (June, 2013) U.S. House. H.R. 1919. *Safeguarding America’s Pharmaceuticals Act of 2013*. <http://www.cbo.gov/publication/44299>

- How are counterfeit and unapproved drugs an unresolved problem on the “demand side?” What is known about this problem?
- What are potential legal and regulatory liabilities associated with the purchase of counterfeit or unapproved drugs (e.g., fraud)?
- How have other enforcement mechanisms played a role in combating this issue (e.g., criminal prosecution, loss of professional licensure, reimbursement policies)? How effective are these mechanisms?

Session II: Identifying Strategies to Improve Communication and Awareness between Stakeholders

- Who are the relevant stakeholders? What are the informational needs of stakeholders?
- Are there mechanisms in place for communicating the public health risks of counterfeit and unapproved drugs to the public?
- Are there mechanisms in place for communicating the professional and legal liability for purchase and use of counterfeit drugs?
- How can communication and education reduce the purchase and use of counterfeits?
- How can communication between stakeholders be improved?
- How have communication initiatives influenced medical practice and purchasing practices?
 - Examples of successful communication campaigns

Session III: Identifying Solutions to Improve Compliance and Professional Behavior

- How can stakeholders collaborate to deter purchasing and dispensing of counterfeit and unapproved drugs in clinical settings?
- How can stakeholders incentivize proper purchasing practices and reporting of improper practices?
- What role can medical boards, professional societies, malpractice insurers, and payers play in reducing the threat of counterfeit and unapproved drugs? How can these stakeholders be supported and engaged by FDA?
- What are the issues and consequences related to reimbursement for counterfeit and unapproved drugs used in clinical settings?

Session IV: Next Steps for Reducing the Threat of Counterfeit and Unapproved Drugs in Clinical Settings

- What practical steps can stakeholders take to implement the solutions or strategies that have been identified?
- What are specific ways stakeholders can begin to collaborate to share information about the purchase and use of counterfeit and unapproved drugs by healthcare providers?