

Reducing the Threat of Counterfeit and Unapproved Drugs in Clinical Settings

Introduction

The use of counterfeit and unapproved drugs, which may contain dangerous substances, incorrect dosages, or no active ingredient, presents a serious public health risk. These illegal and unregulated products may cause patients to experience no change in their disease state in the best case, or severe and potentially fatal complications in the worst case. Although data associated with counterfeit and unapproved drug incidents 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 globally. 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 have revealed counterfeit and unapproved versions of drugs with indications for HIV/AIDS, chronic and acute pain, bacterial infections and influenza, diabetes, high cholesterol, cardiovascular disease, cancer, and others.¹

In response, Congress and a range of federal agencies have worked to address this public health threat. 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.² Currently, Congress is considering national “Track and Trace” legislation which would aid in securing the movement of drugs through the supply chain by creating a system for tracing products.³ In addition, federal agencies have undertaken extensive efforts to secure the drug supply chain and 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.⁴ FDA plays a critical role in this effort, particularly through its Office of Drug Security, Integrity, and Recalls (ODSIR), which works to ensure the quality, integrity, and security of drugs for U.S. patients, as well as through its Office of Criminal Investigations (OCI), which conducts and coordinates criminal investigations regarding the manufacture and sale of counterfeit or unapproved drugs and the illegal diversion of drugs and other FDA-regulated products.

¹ 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>

² Steinbrook R, Sharfstein JM. (2012). The FDA Safety and Innovation Act. *JAMA* 308(14):1437-1438. doi:10.1001/jama.2012.12829.

³ Government Printing Office (June, 2013) U.S. House. H.R. 1919. *Safeguarding America’s Pharmaceuticals Act of 2013*. <http://www.cbo.gov/publication/44299>

⁴ 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.

Many of the ongoing regulatory initiatives to combat counterfeit and unapproved products have focused on key players in the drug supply chain (i.e., “supply side”), 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 knowledge and enforcement of the problem on the “demand side” of counterfeit and unapproved drug purchasing. In particular, the purchase of counterfeit and unapproved drugs by health care professionals has become a growing problem that is neither well understood, nor within the traditional scope of the FDA’s investigation and enforcement practices. In recent years, unscrupulous distributors have specifically targeted clinical settings (e.g., hospitals and physician’s offices) for the sale of physician-administered counterfeit and unapproved drugs, including a variety of injectable drugs.⁵ For example, in 2012 FDA warned 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 authentic version. In response, an investigation was launched to determine who may be responsible for breaching the drug supply chain. FDA proceeded to issue notification letters to over 130 medical practices that were identified as having purchased from an unscrupulous supplier that distributed counterfeit versions of Avastin and/or Altuzan, and also advised the recipients of the public health risks.^{6,7}

In addition to the investigation and potential prosecution of individuals that distribute counterfeit or unapproved drugs, health care professionals who purchase and administer counterfeit and unapproved drugs in a clinical setting can also be investigated and penalized. State boards of medicine have taken a range of actions against health professionals who have knowingly purchased and administered counterfeit and unapproved drugs, including suspension of medical licensure and medical malpractice suits.^{8,9} Health care professionals who falsely bill public and private payers for reimbursement of counterfeit and unapproved drugs may also face prosecution and fines.^{10,11} However, enforcement of professional sanctions against health care professionals who purchase or use counterfeit or unapproved drugs has been inconsistent and sparse, beyond the few cases that are initially investigated and prosecuted by law enforcement agencies.

The broad array of actions that FDA and other stakeholders have taken in addressing the problem of counterfeit and unapproved drugs in clinical settings has helped make important strides in combating

⁵ “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>

⁶ 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>.

⁷ The Partnership for Safe Medicines. (February 05, 2013) Update On Fake Avastin - FDA Warnings in 28 States, Six Prosecutions. Retrieved August 23, 2013, from <http://www.safemedicines.org/2013/01/fda-warnings-in-28-states-six-prosecutions-511.html>

⁸ 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>

⁹ Nevada Medical State Board of Examiners. (November, 2010). Retrieved July 11, 2013, from http://www.medboard.nv.gov/Discipline/Seldon_Stephen.htm

¹⁰ 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>

¹¹ 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>.

the distribution of counterfeit drugs. However, further effort and substantial commitment across multiple health care stakeholders, including health care professionals, licensing boards, professional societies, malpractice insurers, and payers, will be needed to address the incentives for the purchase of counterfeit and unapproved products on the demand side. Leveraging each stakeholder group's distinct knowledge and influence can help reduce demand for drugs that turn out to be counterfeit or unapproved.

To this end, the Engelberg Center for Health Care Reform at the Brookings Institution convened an expert workshop, in collaboration with FDA's ODSIR, to explore potential strategies for reducing the purchase of counterfeit and unapproved drugs, with a particular emphasis on medical professionals within clinical settings. This workshop brought together a broad spectrum of relevant stakeholders, including health care professionals, professional societies, drug manufacturers, state licensing boards, and key content area experts, to understand how stakeholders can create awareness and improve compliance and professional behavior regarding this issue. Over the course of the day, participants discussed current approaches to combating the problem of counterfeit and unapproved drugs, remaining gaps in knowledge and enforcement, strategies to improve communication and awareness among stakeholders, solutions to improve compliance and professional behavior, and next steps for reducing the threat of counterfeit and unapproved drugs in clinical settings. Key themes from the discussion are summarized below.

Creating awareness around counterfeit and unapproved drugs in the clinical setting

While extensive efforts to combat counterfeit and unapproved drugs are underway on the supply side, participants asserted that stakeholders in the clinical setting still lack knowledge and awareness around these issues. Participants stated that a significant portion of physicians who purchased counterfeit or unapproved products were doing so unknowingly, suggesting that physicians may be unsure or unclear about how to identify legitimate distributors to purchase from, what to do if approached by an unscrupulous vendor, or what risks and liabilities are associated with administering counterfeit and unapproved products. As such, greater attention will likely need to be paid to creating awareness around counterfeit and unapproved drugs among physicians, office managers, and others involved in the purchasing and administering of drugs. Participants suggested that stakeholder collaboration will be essential to facilitating education efforts and enabling standardized mechanisms for information sharing among stakeholders. A series of potential strategies were put forth, the main points of which are summarized below.

Use targeted education efforts

Participants highlighted the utility of crafting specific messaging for various health care professionals and stakeholders that may be involved in acquiring, handling, and/or administering counterfeit and unapproved drugs. In particular, participants underscored the need for educational materials that emphasize the incentives and disincentives for each stakeholder group, with a particular focus on physicians, office managers, nurses and allied health professionals, and individuals involved in billing. Additionally, participants noted that certain types of practices (e.g., small, unaffiliated practices) or specialties (e.g., oncology, plastic surgery) may be at a higher-risk of unknowingly purchasing counterfeit and unapproved drugs and, thus, may potentially benefit more from targeted messaging or educational campaigns. Generally, participants found that these education efforts would be most effective if centered on themes that are likely to resonate with health care professionals, including:

- Drug supply chain security;

- Negative consequences for patient safety associated with purchasing outside the legitimate supply chain;
- Financial consequences and negative reputation that could result from purchasing or administering counterfeit and unapproved drugs;
- Legal liability involved in administering counterfeit and unapproved drugs that also could result in criminal charges; and
- Actionable steps they can take if approached by an unscrupulous vendor, or to identify whether drugs they have purchased are illegitimate.

In addition, participants discussed the potential role of payer organizations in reducing counterfeit and unapproved drug use. Participants indicated that directed education efforts that make clear the incentives for payer organizations, particularly within contracting and purchasing groups, may encourage payers to take a more proactive role in creating awareness about counterfeit and unapproved drug purchasing in clinical settings. One potential action that informed payers could take is to leverage existing processes and technologies that payers have to message providers about quality improvement opportunities. These technologies could be configured to enable automatic messaging to providers that are triggered instantaneously once a claim for a product known to be associated with recent counterfeiting is submitted. This would allow for a provider to see a message that counterfeit versions of the administered drug have been identified. The provider could then take further precautions and more closely inspect the product to ensure its authenticity and integrity.

Make important information readily available to health care professionals

Participants suggested that making important information readily available to health care professionals could facilitate the purchase and use of legitimate drugs. Specifically, it was suggested that information on the dangers of purchasing and administering counterfeit and unapproved drugs be included in the mandatory licensure renewal packets that various health care professional licensing boards send out to licensees. This would provide a mechanism for ensuring that every licensed health care professional associated with participating boards receives up-to-date information, for example, about where to send suspicious vendor information, the risks associated with administering counterfeit and unapproved drugs, and a list of resources for health care professionals who would like to be actively involved in surveillance efforts. Participants also added that important information could be pushed out to health care professionals through decision support messages currently in use in clinical settings, alerting the provider that cases of counterfeit and unapproved drugs are currently under investigation or have been found. Participants also stated that health care professionals would be more likely to seek out information regarding the status of a drug (e.g., counterfeit versions found, counterfeit versions under investigation) if such a resource were available. As such, participants recommended the creation of a publicly available and easily accessible database with information regarding the pedigree, legitimacy, and/or FDA warning status of drugs. This would provide an opportunity for health care professionals to improve compliance by making available current information regarding the drugs they administer.

Engage health care professionals in counterfeit and unapproved drug surveillance

Participants stressed that involving health care professionals in counterfeit and unapproved drug surveillance efforts could facilitate significant progress towards a number of objectives critical to reducing demand for these products. Involving health care providers in surveillance and reporting activities could serve as a mechanism to further provide health care professionals with information regarding counterfeit and unapproved drugs, and act as another way of educating health care professionals about the risks associated with their purchase and use. Participants pointed out that engaging health care professionals in these efforts would create active advocates for increasing

awareness around counterfeit and unapproved drugs. Furthermore, participants underscored that by engaging a strong network of health care professionals in surveillance and reporting, the amount and quality of data captured about counterfeit and unapproved drug advertising, purchase, and usage would be enhanced and a more complete understanding of the magnitude of this issue could emerge.

Publicize ways health care professionals and FDA can exchange information

Participants expressed concern that many health care professionals, if approached by unscrupulous vendors through blast faxes or who observe suspicious drug labeling on purchased products, may not know where to go for additional information or to whom to forward the information. Participants suggested that mechanisms for sharing this information (e.g., Medwatch for adverse events, contacting OCI for forwarding suspicious faxes) should be widely publicized as part of any education campaign.* Additionally, participants noted that by making this information widely available to health care professionals, the amount of data on counterfeit and unapproved drugs that FDA receives could increase, allowing FDA to identify illegitimate distribution operations more quickly and relay that information to health care community sooner.

Create publicity around practices found to use counterfeit or unapproved drugs

Participants underscored the need to draw the health care community and public's attention to investigations and court cases around medical practices allegedly purchasing or administering counterfeit and unapproved drugs. Participants specifically highlighted the importance of emphasizing the consequences of these actions, particularly with regards to negative impacts on reputation and associated criminal penalties, as a way to educate health care professionals about the issue and its consequences, and to provide a visible deterrent for health care professionals.

Engage patients and the public

Participants explored a set of strategies to improve patient and public awareness of counterfeit and unapproved drug use, and to encourage active participation in combating this issue. One strategy discussed was the need to specifically gear education efforts so that patients and the public become aware of the dangers of certain practices (e.g., leaving the secure supply chain for products, purchasing drugs from other countries, brown bagging from illegitimate distributors). Participants added that encouraging patients to ask for information specific to their medication prior to injection or administration (e.g., in the form of a handout), such as what the source of their medication is, whether there any known side effects and other important information, may be another useful way to engage patients in their care. However, concern was expressed that communications meant to increase awareness of counterfeit and unapproved drugs could discourage adherence to medications or decrease overall trust in health care professionals. Thus, special attention will likely need to be paid to developing balanced communications that ensure patients are aware of the risks while preventing excessive fear. In addition, participants described the need for new, innovative ways to engage patients and the public in drug safety, and increase reporting of issues related to suspected counterfeit and unapproved drugs. One example presented was the possibility of patients using a mobile device such as a mobile phone to take a picture of their medication vial and upload it through a phone application. This application could then alert the patient if the medication has any FDA warnings issued, or make it easier to submit information if the patient has reason to suspect the drug's legitimacy or experiences any adverse side effects after administration.

Addressing professional behavior and compliance regarding counterfeit and unapproved drugs among health care professionals

In addition to creating awareness among stakeholders, participants discussed the need for complementary strategies to improve professional behavior and compliance among health care professionals. Participants noted that while many health care professionals may purchase and administer counterfeit and unapproved drugs unknowingly, some health care professionals may do so knowingly and intentionally. As such, participants emphasized the need not only to deter the purchase and use of counterfeit and unapproved drugs, but also to incentivize health care professionals to seek and administer drugs from legitimate sources. Strategies that emerged as prominent themes of the discussion are summarized below.

Disincentivize the purchase and administration of counterfeit and unapproved drugs

Participants explored a range of potential strategies to deter the purchase and use of counterfeit and unapproved drugs by health care professionals. One example considered by participants was to tie claims reimbursement for physician-administered drugs to proof of the legitimacy of the drugs source. Participants pointed out that this solution would only be possible if a unique identifier for drugs could enable the authentication of the drug at the point of administration. Another deterrent suggested during the discussion was to increase criminal penalties for the administration of counterfeit and unapproved drugs, particularly by adding time in prison to existing monetary fines. Participants also suggested a national provider disciplinary action databank that would aggregate information about disciplinary actions taken against providers into one searchable, publicly accessible database. This potentially creates a deterrent effect, as health care professionals would take into account the potential negative effect on professional reputation and licensing of being disciplined for purchasing and administering counterfeit and unapproved drugs. Participants emphasized that while each of these efforts will be important in deterring improper behavior on the part of health care professionals, they must also be balanced with education to create awareness about the issue of counterfeit and unapproved drugs.

Provide health care professionals with adequate incentives to buy legitimate drugs

Participants examined a range of incentives to encourage health care professionals to buy from legitimate sources within the secure supply chain. One incentive put forth is to ensure that reimbursement for providers is stable and adequate so that health care professionals do not feel financially pressed to go outside of the secure supply chain for cheaper alternatives. Additionally, participants indicated that providing flexibility for shortages and timely adjustments for fee schedules would be beneficial to providers and may help ensure that providers are not under any pressure to consider unregulated sources that may lead to the purchase of counterfeit and unapproved drugs. Participants also added that engaging with health care professionals who have purchased from a vendor that has sold counterfeit or unapproved drugs in a discussion about the risks could help bring these providers back to buying from legitimate distributors.

Conclusion

This meeting began an important conversation around reducing the threat of counterfeit and unapproved drugs in clinical settings. Participants identified critical points, over-arching goals, and concrete strategies to increase awareness about this issue, and improve the professional compliance of health care professionals in this regard. Some of the key strategies include:

- Use targeted education efforts to engage physicians, office managers, patients, payers, and other relevant stakeholders and create awareness about counterfeit and unapproved drugs;
- Improve data around counterfeit and unapproved drugs by engaging health care professionals in surveillance efforts;
- Provide health care professionals with easily accessible and readily available information about counterfeit and unapproved drugs; and
- Create financial and other disincentives (e.g., tie claims to drug legitimacy) for health care professionals to deter the purchase and administration of counterfeit and unapproved drugs.

While it is clear that each stakeholder group will have an important role to play in this effort, a clear, multi-pronged approach that takes into account the resources of each stakeholder group will be needed to make substantial progress towards decreasing the demand for counterfeit and unapproved drugs in clinical settings.

*Note: To share suspicious activity with FDA related to possible unapproved/counterfeit drugs or suspect faxes from distributors, email drugsupplychainintegrity@fda.hhs.gov, contact OCI <http://www.accessdata.fda.gov/scripts/email/oc/oci/contact.cfm> or fax 301-847-8722 Attention: Division of Supply Chain Integrity (DSCI). For general questions for the Office of Drug Security, Integrity and Recalls, call 301-796-3130.