

## Oncology and the Internet: Regulatory Failure and Reform

By *Tim K. Mackey, MAS, and Bryan A. Liang, MD, PhD, JD*

California Western School of Law; University of California, San Diego School of Medicine; and San Diego State University School of Public Health, San Diego, CA

Drug shortages have emerged as a serious patient safety and public health crisis and are affecting a variety of drug classes.<sup>1</sup> This includes a number of generic sterile injectables that are used to treat various forms of cancer.<sup>2-4</sup> There are multiple causes associated with the oncology drug shortage, but the primary factors are economic, driven by pricing pressures from payers (such as Medicare) that make profitable production of these drugs challenging.<sup>4</sup> Indeed, limited incentives for generic production of low-profit cancer drugs and reimbursement declines have also led to declines in production, increased use of more expensive and less effective brand drugs, and ultimately shortages of essential low-cost medicines.<sup>4</sup> The result has been increased stress on existing scarce production lines, which can at any time be adversely affected by shortages of active pharmaceutical ingredients, technical and manufacturing problems, and regulatory issues such as noncompliance and need for corrective action.<sup>5</sup> This lack of system redundancy can lead to critical halts in supply, with patients delaying or foregoing treatment or substituting therapies in shortage with expensive and/or risky alternatives.<sup>3,4</sup> These already precarious conditions are worsened by an unregulated gray market and burgeoning illicit online marketplace distorting demand, which urgently needs more attention and reform.

With the oncology drug shortage as the primary consequence of the failure of the traditional drug supply chain, providers and patients may seek other alternatives for sourcing. This includes the disturbing consequence of purchasing drugs in shortage from the gray market, a secondary wholesaler system known to be risky. Here, drugs are offered at exorbitant mark-ups of up to 3,000% via often daily solicitations (fax, telephone calls, e-mails) made directly to providers; they may be of questionable quality and/or safety and may be counterfeit, as demonstrated in the past with cancer therapies.<sup>4,8</sup> Indeed, patient death, as in the case of a woman with breast cancer who was administered one of 25,000 counterfeit versions of erythropoietin, has been associated with cancer medicines that may have been adulterated passing through the secondary market.<sup>10</sup> Most recently, counterfeit versions of the injectable chemotherapy drug Avastin (bevacizumab; Genentech, South San Francisco, CA) have been detected and may have been introduced in more than 19 medical practices in California, Texas, and Illinois.<sup>11</sup> Sourcing of this counterfeit medicine occurred globally, including through wholesalers and distributors in Turkey, the United Kingdom, Switzerland, Egypt, Denmark, and Barbados, before finally arriving in the United States.<sup>12</sup> Not only did the coun-

terfeit product contain no active pharmaceutical ingredient, but one of the gray market suppliers had earlier sold other cancer drugs including pegfilgrastim and fulvestrant at deeply discounted prices, which is highly suspect.<sup>11</sup>

Ongoing shortages may lead desperate patients to another and potentially more dangerous and little-discussed source of drug safety regulatory failure: the Internet. The Internet has poor regulatory oversight, leading to highly prevalent illicit drug marketing and sales.<sup>13</sup> Nevertheless, shortage situations have led to providers purchasing from suspect Internet sources, and at least 2.9% to 13% of patients have admitted to buying drugs online, despite global public health warnings.<sup>14,15</sup> These vendors may promote purchases without a prescription and represent a significant patient safety risk, given the high prevalence of counterfeit medicines<sup>13</sup> and the complex nature of cancer biologics, which are sensitive to transport and storage, even assuming authenticity.

The combination of diversion and online sales is a global health concern for patients with cancer. The discovery of counterfeit bevacizumab was but one in a string of detections of counterfeit cancer treatments, including contaminated leukemia drugs detected in China, fake cancer drug distribution in the United Kingdom, and an individual sentenced to 33 months in prison for selling a fake “experimental cancer drug” over the Internet.<sup>16-18</sup> These counterfeit cancer drugs provide an indication of the global scope of the problem.

In addition, questionable sources of advertising can mislead patients about the benefits, risks, legality, and authenticity of cancer treatment. Importantly, illicit online vendors have taken full advantage of the Internet, moving nimbly from search engines to popular social media such as Facebook, Twitter, YouTube, and others to target oncology patients and treatments<sup>19-21</sup> and have also extended oncology advertising to suspect screening tests.<sup>22</sup> The resulting system is a parallel, unaccountable one without professional guidance or appropriate clinical care for oncology patients.

For example, one Google search conducted on November 26, 2011, for “anticancer drugs online” produced—as the second result—a YouTube video advertising “Buy anticancer drugs online” (<http://www.youtube.com/watch?v=xEICZiK7zTY>). The video advertises both branded and generic anticancer medicines at the “cheapest” prices and offers a link for purchasing ([www.Way2rx.com](http://www.Way2rx.com)). The link leads consumers to a Web site offering more than 100 oncology products online, including cancer shortage drugs doxorubicin, bleomycin, cytarabine, docetaxel, and leucovorin (ie, US Food and Drug Administration

[FDA] shortage drugs for oncology). The site seems to originate in India, and all identified products are offered for sale without a prescription. These factors point to the significant safety risks of this vendor.<sup>13</sup> Beyond the YouTube marketing, the Web site is strategically complemented by a widget to link to a user's Facebook site, by a Twitter page (<https://twitter.com/#!/way2rx>), and by its other social media links to engage and attract consumers.

Such marketing illustrates the tremendous risks faced by oncology patients. First, it is unlikely that this vendor has cancer drugs currently in shortage, given the nature of this global concern. But second, even if vendors did have access, it is unlikely they would have the technical knowledge necessary to transport sensitive drugs and biologics often used in cancer care, which require specialized handling, cold storage, and other key efficacy concerns.<sup>22</sup> Finally, it should also be noted that the importation of cancer drugs sourced from outside the United States is generally not permitted unless the product is unavailable commercially in the country, and there is a physician overseeing treatment with the imported drug.<sup>1</sup>

The combination of collective regulatory failure in the drug shortage policy, the gray market risks, and the sourcing of drugs via illicit online pharmacies represents a serious threat to patients with cancer. In the absence of meaningful regulation and enforcement of Internet-based advertising, and with the failure of the FDA to address social media-based advertising, US regulators and policymakers need to address urgently the combined risk of cancer drugs in shortage and illicit online sales.

Making all Internet drug sales illegal except for entities accredited through the National Association of Boards of Pharmacy Verified Internet Pharmacy Practice Site (ie, VIPPS) program—the only program recommended by the FDA—would be an important safety benefit for oncology patients. Furthermore, the FDA and Department of Justice should use injunction power to prevent questionable Web vendors from misleading promotions regarding cancer screening and treatments. This would promote patient safety as well as protect against exploitation of desperate cancer treatment needs and ensure accountability for these actions. This short-term strategy would build on recent efforts by the European Union to address suspect online drug vendors.<sup>23</sup>

However, long term, the focus on international cooperation through legal means, such as the recent MEDICRIME convention seeking signatories to address the safety of the global drug supply, is also a positive sign.<sup>24</sup> Other initiatives such as global

public-private partnerships can be incorporated into such continuing efforts; for example, in Operation Pangea III, 45 countries, nongovernmental organizations, global law enforcement, the private sector, and public health entities combined to shut down hundreds of illicit Web sites selling high-risk drugs, including oncology drugs.<sup>25</sup> However, maintenance and adjustment of these efforts and approaches are required because of the rapid adaptability of illicit sellers to exploit gray market vulnerabilities as well as the limited risks of engaging in online sales.<sup>25</sup> Oncologists, patients with cancer, and policymakers should be aware of these systemic concerns, maintain and update patient safety systems, and cooperate internationally to address this global public health issue.

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*Corresponding author: Tim K. Mackey, MAS, Senior Research Associate, Institute of Health Law Studies, California Western School of Law, 350 Cedar St, San Diego, CA 92101; e-mail: [tmackey@ucsd.edu](mailto:tmackey@ucsd.edu).*

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## References

1. Shortages of cancer drugs in the USA. *Lancet Oncol* 12:313, 2011
2. IMS Institute. Drug shortages report. <http://www.imshealth.com/portal/site/ims/menutitem.edb2b81823f67dab41d84b903208c22a/?vgnextoid=a6fbcc0f68f73310VgnVCM100000ed152ca2RCD&vgnnextfmt=default&vgnnextrefresh=1>
3. Kaiser J: Shortages of cancer drugs put patients, trials at risk. *Science* 332:523, 2011
4. Gatesman ML, Smith TJ: The shortage of essential chemotherapy drugs in the United States. *N Engl J Med* 365:1653-1655, 2011
5. Ventola CL: The drug shortage crisis in the United States: Causes, impact, and management strategies. *P&T* 36:740-757, 2011
6. Reference deleted.

7. Reference deleted.
8. Institute for Safe Medication Practices: Gray market, black heart: Pharmaceutical gray market finds a disturbing niche during the drug shortage crisis. <http://www.ismp.org/Newsletters/acutecare/showarticle.asp?ID=3>
9. Reference deleted.
10. Eban K: *Dangerous Doses*. New York, NY, Mariner Books, 2006, p 504
11. Moisee K: Cancer patients furious over counterfeit Avastin. <http://abcnews.go.com/Health/CancerPreventionAndTreatment/cancer-patients-furious-counterfeit-avastin/story?id=15629540#.T03g0cz5wdl>
12. Faucon B, Whalen J: Fake Avastin took murky path to U.S. <http://online.wsj.com/article/SB10001424052702303302504577323500453577094.html>
13. Liang BA, Mackey T: Searching for safety: Addressing search engine, web-

site, and provider accountability for illicit online drug sales. *Am J Law Med* 35: 125-184, 2009

14. Orizio G, Merla A, Schulz PJ, et al: Quality of online pharmacies and websites selling prescription drugs: A systematic review. *J Med Internet Res* 13:e74, 2011

15. Mazer M, DeRoos F, Shofer F, et al: Medications from the Web: Use of online pharmacies by emergency department patients. *J Emerg Med* 42:227-232, 2012

16. Hooker J, Bogdanich W: Tainted drugs tied to maker of abortion pill. <http://www.nytimes.com/2008/01/31/world/asia/31pharma.html?hp>

17. Five in court over "EU's most serious fake medicine scam." <http://www.independent.co.uk/news/uk/crime/five-in-court-over-eus-most-serious-fake-medicine-scam-2152769.html>

18. US Department of Justice: Canadian man sentenced to 33 months in prison for selling counterfeit cancer drugs using the Internet. <http://www.justice.gov/opa/pr/2010/August/10-crm-958.html>

19. Liang BA, Mackey TK: Prevalence and global health implications of social media in direct-to-consumer drug advertising. *J Med Internet Res* 13:e64, 2011

20. Liang BA, Mackey TK: Online availability and safety of drugs in shortage: A descriptive study of internet vendor characteristics. *J Med Internet Res* 14:e27, 2012

21. Liang BA, Mackey TK: Vaccine shortages and suspect online pharmacy sellers. *Vaccine* 30:105-108, 2012

22. Lovett KM, Liang BA, Mackey TK: Risks of online direct-to-consumer tumor markers for cancer screening. *J Clin Oncol* 30:1411-1414, 2012

23. European Healthcare Fraud and Corruption Network: EU policy on counterfeit medicines. <http://www.ehfcn.org/eu-corner/eu-policy/counterfeit-medicines/>

24. Watson R: Governments pledge to clamp down on counterfeit drugs. *BMJ* 343:d7096, 2011

25. Mackey TK, Liang BA: The global counterfeit drug trade: Patient safety and public health risks. *J Pharm Sci* 100:4571-4579, 2011



## Cancer.Net Mobile App for Patients

Described as "a gem of a freebie," Cancer.Net's new app is the mobile companion for patients to stay informed about cancer and to organize important personal data often needed for visits to physicians. It includes interactive tools to help patients get answers to important questions, track adverse effects, and manage medications.

Direct your patients to [cancer.net/app](http://cancer.net/app) to download the Cancer.Net mobile app.



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