



Stop the War on Drugs

By Scott Gottlieb, M.D.

In December 2005, Eli Lilly pled guilty to a criminal indictment from the Justice Department and paid \$36 million in fines and “disgorgement” of its ill-gotten gains. The company’s crime was mounting a concerted effort to inform doctors that, according to leading medical authorities, the firm’s estrogen-modulating drug Evista substantially reduced the risk of invasive breast cancer in postmenopausal women.

The finding came from a series of landmark national studies, some eventually touted by government research. So why the criminal charge?

At the time Eli Lilly was conveying the cancer information to doctors, the Food and Drug Administration (FDA) had approved Evista for treating osteoporosis, not preventing cancer. Only this past September—eight years after the first significant cancer prevention results were published—did the FDA approve Evista for use against breast cancer, turning Eli Lilly’s crime, by some measures, into a public service.

For patients and doctors who rely on the latest clinical information to make hard decisions, no relevant scientific discovery took place between the medical findings, the legal prosecution, and the FDA’s approval of those same results. In fast-moving fields like cancer, in which doctors tailor treatments based on evidence that is constantly evolving, two years can be an eternity to learn about important science. For some patients, that interval can be fatal.

At issue is what is referred to as “off-label promotion”—allegations that drug companies encourage doctors to use medicines for purposes not yet approved by the FDA. These charges are applied even when the information drug firms

are sharing is part of educational meetings, peer-reviewed journal articles, or treatment guidelines issued by medical-specialty societies and government researchers.

The prosecutions are aimed at recouping federal money. The argument is that the medical community is goaded by the drug companies into filing “false claims” with the government, and hospitals and health plans charge Medicare and Medicaid for drugs used for unapproved indications.

Drug firms tend to settle these cases. Firms have good reason to cut a deal: if they fight and lose in court, they can be banned from doing any business with government programs like Medicare. At one time, prosecutions were aimed at a handful of bad actors that encouraged prescriptions for purposes far outside popular medical practice. But like a lot of government efforts, the scope of these prosecutions expanded to encompass a much broader slice of medical activity.

The Justice Department rarely alleges in these cases that the scientific information is false or misleading, only that a firm can be “ahead of the science” in sharing information with doctors about emerging uses of medicines, even when those new uses quickly become the mainstay of care. Underlying this, of course, is a nagging presumption that doctors cannot be trusted to weigh for themselves this sort of medical information and thus need the FDA’s supervision.

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This might be more tolerable in a world where the FDA rapidly adjudicates study results to decide what belongs in and out of drug labels. In reality, the FDA reserves ten months to consider supplemental uses for marketed drugs, and the entire process usually is much longer. In many cases, doctors do not easily learn about these new drug uses or get targeted education on prescribing without the help of the drug firm, which is the only deep-pocketed actor with an incentive to share this kind of information.

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The Philadelphia U.S. attorney’s office has conducted a multiyear investigation into the biotech company Genentech. They are alleging that meetings the company sponsored for oncologists in the 1990s were illegal—because Genentech shared information about unapproved uses for its drug Rituxan, used largely in the treatment of lymphoma. Nevermind that the forms of lymphoma for which Rituxan was to be used were largely fatal; that some of those uses are now approved by the FDA; and that the education was based on findings from large studies, including one supported by the government. In fact, if you queried the National Cancer Institute’s website—even at the time when Genentech allegedly engaged in the illegal educational activity—for advice on the best treatments for some of these same forms of lymphoma, the search returned “Rituxan.”

“Off-label” is now a dirty term in the conventional lexicon, made synonymous with lawbreaking as a result of these prosecutions, even though it describes the way more than half of cancer medicine is practiced. It is true that some off-label drug use is based on very unsettled science and has more risks. But medicine—and not just cancer care—involves lots of hard choices. And the more serious the disorder, often the more likely it is that for every right and wrong treatment choice there are many other practical decisions painted in shades of gray. Efforts to confine patients and doctors to FDA-approved uses have their own health consequences, raising the

question: just who is in the best position to make these hard choices?

The travails of another Genentech drug, the breast cancer medicine Herceptin, demonstrate the health consequences of these prosecutions. Herceptin was widely used in advanced breast cancers for years, and recently it was found to cut recurrence by about half in some patients with earlier-stage tumors. The results were first published early in 2005, and the new use was approved by the FDA in late 2006. The wider use of Herceptin will save lives, but doctors did not embrace it right away.

Herceptin prescriptions spiked when the study was first published in the *New England Journal of Medicine*, only to tail off before spiking again at the time of FDA approval. Those early adopters were probably familiar with the drug and the findings, perhaps through practicing in busy academic centers. Some of the late adopters might have been reluctant to take up the new use without the benefit of targeted education. You can bet that folks at Genentech, living under the thumb of the Philadelphia U.S. attorney, were not about to talk up the landmark findings.

The use of Herceptin in early-stage breast cancers was roughly half what you would expect for the almost two years between publication of the study’s findings and the FDA nod. It is hard to deny that some of those Herceptin-eligible women who did not get the drug are now unnecessarily doomed.

Attorney General Michael Mukasey could add to the staff manual for his attorneys a requirement that they merely check with a public health authority like the National Institutes of Health to see if a certain off-label use falls within the scope of appropriate medical care before waging a legal war. Even that may be a hard sell in Washington, where prosecutions are pursued on the basis of how much money they can recoup.

This month, Representative Henry Waxman (D-Calif.) took umbrage at a copy of a draft FDA guidance (he leaked it himself), saying that, as a public health matter, the FDA found it appropriate for drug firms to share study reprints from peer-reviewed medical journals. Drug firms are *personae non gratae* in Washington, a result of the industry’s own excesses but also of a lot of political targeting. The result is an anything-that-bashes-pharma-goes mentality in policymaking.

Politicians wage broad wars on medicine to claim thin strips of ideological terrain. This would be good political theater if there were not so many human victims.