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FDA Censorship Wins $36 Million in Fines and Penalties

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The federal Food and Drug Administration (FDA) recently won a case against Eli Lilly & Co. when the company agreed to plead guilty and pay $36 million in connection with illegal promotion of its pharmaceutical drug Evista. What did the company do to earn such a penalty?

The company illegally promoted its pharmaceutical drug Evista because Lilly employees had advocated the product for "off-label" uses. Evista was approved for the treatment of osteoporosis, but the company was not allowed to breathe a word that Evista might be good for something else. The company did have evidence for the prevention of breast cancer and heart disease, but according to the federal Food, Drug, and Cosmetic Act, as interpreted by FDA regulations, promotion of these other uses was forbidden.

Two research articles were published in the *Journal of the American Medical Association* (JAMA), a prominent peer-reviewed scientific journal that presented scientific data supporting the use of raloxifene (the chemical name for Evista) for breast cancer prevention and heart protection. The first article was published in 1999, and it showed that raloxifene "reduced the risk of invasive breast cancer by 76% during three years of treatment." This was a substantial study that ran from 1994 through 1998 at 180 clinical centers in twenty-five countries, primarily the United States and countries in Europe, and included a total of 7,705 postmenopausal women with osteoporosis as the subject population. A "secondary analysis" of the same 7,705 women was published in 2002, and it demonstrated a "lower risk of cardiovascular events" for a subset of 1,035 women in the study who had an increased cardiovascular risk when the study began.

One would expect that a favorable study like this -- in a peer-reviewed scientific journal of the highest quality -- would be greeted enthusiastically by the medical profession and the FDA. However, the FDA does not sanction promotion of any so-called "off label" uses, and companes that do promote them risk severe penalties. Eli Lilly got caught.

According to the U.S. Department of Justice's December 21, 2005 press release announcing the Lilly settlement, Lilly sales representatives "were trained to prompt or bait questions by doctors in order to promote Evista for unapproved uses." The Department of Justice charged that the company was also holding "consultant meetings" for physicians during which the unapproved uses of Evista were discussed.

Why do the FDA and the Justice Department care so much about stopping the distribution of truthful scientific information? The DOJ said the rationale for "prosecuting the illegal marketing of pharmaceutical drugs" was that "promotion by a pharmaceutical company of unapproved uses of a product challenges the drug approval process." The FDA's acting director added that the penalties

"demonstrate that there is a strong system in place for ensuring that pharmaceutical companies fully comply with all aspects of the drug approval process."

Regulatory Approval and the Peer-Review Process Are Not the Same

The core of FDA regulatory authority is the agency's ability to prevent distribution of information by pharmaceutical manufacturers. By limiting the promotion to only the "approved" indications for a product, FDA can compel pharmaceutical companies to generate and submit data through cumbersome and expensive submissions (Supplemental New Drug Applications), then force them to wait while the agency reviews the data and approves or disapproves the "new indication."

Notice the difference between publication of a clinical study in a reputable scientific magazine and the lengthy process it takes to get a new indication approved by the FDA. Peer-reviewed scientific research is deemed worthy of publication, and this is the widely accepted standard for the presentation of scientific information. If a physician sees a peer-reviewed scientific article about a drug in a medical magazine, then consideration of the results of such a study can influence medical decisions to prescribe it. However, if pharmaceutical company representatives present the same information -- even circulating a reprint of the journal article -- they may be subject to civil and criminal penalties.

Off-label prescribing is an entirely legal and reputable medical practice. It is perfectly acceptable for a physician to use any FDA-approved drug in any way that he or she believes can benefit the patient, prescribing accordingly. As one court decision described, in some circumstances an off-label use of a particular drug "may even define a standard of care" because the "pace of medical discovery runs ahead of the FDA's regulatory machinery."

So, who cares if drug companies are prevented from informing doctors about additional uses of their products? The drug companies are obviously highly motivated to distribute favorable scientific information about their products because they can make more sales, and FDA rules block the claims because the agency's regulatory power rests on this ability. What difference does this regulatory struggle make? It could make a big difference -- to patients.

In the late 1990s my mother, Inge Flynn, was dying of advanced breast cancer. In 1999, the Evista cancer study was published in JAMA. I wonder: if my mother's doctors had known of the raloxifene study, would they have prescribed it during her illness? Might the "off-label" drug Evista have benefitted her? She died on September 30, 2000.

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