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Drugmakers push for looser off-label rules

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Drug advertising can alter the practice of medicine, which makes health advocates wary of promotional practices such as TV spots aimed at patients.

Now, consumer groups fear that drug companies will soon win permission to use a seemingly sober and impartial source of information - scientific research articles - to publicize new uses for their products.

The pharmaceutical industry is pressing the Food and Drug Administration for greater freedom to give doctors copies of scientific studies about experimental uses of their drugs - that is, to treat diseases not already included on the drug's FDA label. And the FDA is considering lighter restrictions.

Industry advocates say the reprints would provide physicians with the most up-to-date information about emerging new uses of drugs well before the FDA can approve them. But industry critics say the results would be disastrous - warping prescribing patterns, undermining the authority of the FDA, and corrupting the biomedical research enterprise.

Those sweeping concerns might seem mystifying to consumers unaware of the powerful role played by medical journal articles in determining the use of drugs.

Mere studies of experimental or "off-label" uses of approved drugs would have no effect on treatment if not for a quirk of the U.S. drug regulatory scheme unknown to many patients. When evidence arises for new uses of approved drugs, that use can find its way into medical practice in two ways.

The government's preference is for drug manufacturers to conduct rigorous clinical trials in the additional disease, then ask the FDA to add the new condition to the medicine's label. That expanded approval prompts doctors to try the new remedy and influences health plans to pay for it. Until the FDA grants approval, the drugmaker is forbidden to promote the product in the additional disease.

Doctors free to prescribe

A second, informal route allows a new drug use to be adopted by the medical community without

FDA approval.

Once the FDA approves a drug for one disease, doctors are free to prescribe it off-label for any other condition. In most cases, the FDA has no authority over the practice of medicine.

Off-label prescribing can be beneficial, and in many cases, doctors have no choice. Some rare illnesses have no approved remedy, for example. Physicians search medical literature for evidence that a drug approved for a different disease will work for the rare condition. Scientific articles and compilations of medical studies called compendiums also can persuade health insurance companies to pay for treatments not reviewed by the FDA.

Drug companies couldn't legally promote off-label uses. But many of them did so anyway, according to state and federal prosecutors who have won felony convictions and millions in fines from pharmaceutical firms in investigations of off-label promotion campaigns over the past five years.

Their probes uncovered evidence that manufacturers often relied on scientific journal articles to drum up those sales, in an end run around the government prohibition against outright advertising of off-label uses. The tactic also allowed companies to bypass the expensive FDA approval process for new uses.

State prosecutors joined the protests when the FDA announced this year that it may ease restrictions on manufacturers that want to pass out copies of scientific studies about experimental uses to physicians.

The proposed FDA rules would allow drugmakers to pitch their products off-label based on poor or misleading research while avoiding the expense of rigorous trials needed for FDA approval, Illinois Attorney General Lisa Madigan and Oregon Attorney General Hardy Myers said in comments to the FDA.

Watchdogs question change

"As a result, medical expenditures for unnecessary or even harmful drugs will be increased, and scientific study of possible new uses of approved drugs may be discouraged," the prosecutors said. "Drug manufacturers have promoted their products for off-label uses even when the FDA has denied the application for the off-label use because the use was unproven or too risky."

Drug watchdog groups, health plans and prosecutors say the FDA is preparing to ease the rules amid a flood of evidence that manufacturers have distorted their own research results in scientific journals, selectively released positive studies while suppressing unfavorable data, and used ghostwriters to conceal their role in publications.

The American Medical Association, while supporting the distribution by manufacturers of accurate

and unbiased studies from independent sources, said "very troubling questions have been raised regarding pharmaceutical companies' manipulation of the peer-review medical journal process to promote their products."

"The industry practices that have been identified threaten the credibility of the entire peer-review journal process," Michael Maves, chief executive of the AMA, wrote in comments to the FDA. "Such practices call into question whether physicians, patients and the public can be assured that information provided is accurate and unbiased."

Many of the industry critics want the FDA to revive former regulations that lapsed in 2006. Those rules barred drugmakers from distributing articles about experimental uses unless they also promised to submit the new use for FDA approval, and provided the articles for the agency's inspection.

The agency's newly proposed guidelines instead would allow manufacturers to freely distribute "adequate and well-controlled clinical investigations," published in peer-reviewed journals, that have not been written or influenced by the maker of the product studied.

Trade associations for drugmakers and biotechnology companies say the tentative FDA guidelines are a step in the right direction. The Pharmaceutical Research and Manufacturers of America, or PhRMA, said drugmakers have the time and resources to monitor medical literature for the most up-to-date information and distribute it to busy doctors who have little time to conduct such inquiries.

"Simply put, no information source can be expected to track the medical literature on a given medicine more comprehensively than a manufacturer that researches and develops the product," the organization said in comments filed with the FDA.

Studies useful, firms say

But industry groups say the proposed rules are still too restrictive. They want the FDA to change wording that would allow manufacturers to distribute only "adequate and well-controlled clinical investigations" not influenced by the drug's maker.

Company advocates maintain that physicians can draw valuable information from articles about manufacturer-funded studies; studies that are not double-blinded to eliminate bias; and those that include no control group for comparison, or in other ways do not meet the FDA's standards for the clinical trials that must be submitted for approval of a new use.

The tentative FDA guidelines include attempts to make sure the information distributed by manufacturers includes a balanced view of the risks and benefits of a new drug use. The drugmaker must attach the FDA-approved label of the product discussed in the distributed article, which must

bear a prominent disclaimer stating that it covers unapproved uses. Companies could not give out articles the FDA has found inaccurate or misleading.

Those provisions went unchallenged by the Washington Legal Foundation, a legal policy center that has battled with the FDA in court for years over the limits on off-label promotion. But the foundation said other proposed restrictions would violate the free speech rights of biomedical companies. The FDA cannot require companies to provide a bibliography of articles on the same unapproved use, or to attach studies critical of the article distributed, the organization said. Nor can the agency rule out any study unless it believes the article has "absolutely no scientific value," the organization said.

Such limits would violate the terms of a 1999 injunction that resulted from the foundation's past court challenges of FDA restrictions, it said. The Washington Legal Foundation "intends to ensure compliance with its injunction and will seek contempt of court citations against FDA officials who violate its terms," the organization's attorneys said in comments filed with the FDA.

The period to submit comments on the proposed guidelines to the FDA ended April 21, and the agency has no set timeline to release its final guidelines.

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