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FDA Urged Withholding Data on Antidepressants

Makers Were Dissuaded From Labeling Drugs as Ineffective in Children

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The Food and Drug Administration has repeatedly urged antidepressant manufacturers not to disclose to physicians and the public that some clinical trials of the medications in children found the drugs were no better than sugar pills, according to documents and testimony released at a congressional hearing yesterday.

Regulators suppressed the negative information on the grounds that it might scare families and physicians away from the drugs, according to testimony by drug company executives. For at least three medications, they said, the FDA blocked the companies' plans to reveal the negative studies in drug labels, and in one case the agency reversed a manufacturer's decision to amend its drug label to say that the drug was associated in studies with increased hostility and suicidal thinking among children.

"Why would FDA require a company to remove stronger labeling?" demanded an incredulous Rep. Greg Walden (R-Ore.) yesterday, at a hearing of the House Energy and Commerce subcommittee on oversight and investigations. "FDA should want to encourage a company to do that kind of thing."

Janet Woodcock, FDA's deputy commissioner for operations, responded that regulators believe the jury is still out on the drugs. The negative trials, she said, did not mean the medications were ineffective.

Several representatives noted that the study results were obtained at tremendous cost to the American public because Congress granted companies profitable patent extensions as an incentive to conduct the trials.

Rep. Henry A. Waxman (D-Calif.), a member of the subcommittee, said it was absurd to give companies profitable patent extensions on their drugs to encourage the trials and then limit dissemination of the results. He said his staff had estimated that a patent extension given to Pfizer Inc. was worth $1 billion dollars. Wyeth Pharmaceuticals, he said, made $500 million.

The hearing was prompted by widespread complaints that crucial information about the safety and effectiveness of antidepressant medications had not been communicated to physicians and the public. More than two-thirds of all studies of antidepressant use among depressed children have failed to show the drugs are effective.

Prozac is the only medicine to be specifically approved to treat children's depression, but a number of other drugs are widely prescribed.

Most physicians have not had access to the negative data and are prescribing the drugs to millions of American children largely because the drugs have proved effective among adults. Two internal FDA analyses recently concluded that the class of medications is associated with an increased risk of suicidal behavior among children.

At the hearing, Pfizer Vice President Cathryn M. Clary testified that FDA had told the company that existing language in the label for Zoloft, which suggested "that efficacy has not been established" for depressed children, was sufficient. Pfizer had planned to add that two studies of Zoloft found the medication was no better than sugar pills.

"We do not feel it would be useful to describe these negative trials in labeling," FDA officials wrote in a letter to the company, "since these may be misinterpreted as evidence that Zoloft does not work."

FDA's Woodcock said agency officials had told Wyeth to scale back a label change that warned that the drug Effexor had been linked to suicidal thoughts, hostility and self-harm.

"It was not very understandable," Woodcock said in an interview when asked why the FDA had found the Wyeth label objectionable.

Wyeth and other companies were instead asked to insert a general caution that physicians should carefully monitor the risk of suicide among all patients with depression. Agency officials said at the time that the caution was a reiteration of good clinical practice.

Joseph S. Camardo, senior vice president at Wyeth Pharmaceuticals, said company scientists had disagreed with the FDA on how to interpret the data in its labeling.

"We thought our proposal was reasonable, so it was a bit of a surprise," he said of the FDA ruling that substituted a less pointed warning.

In the agency's most recent internal review of the antidepressant studies, FDA scientist Tarek Hammad concluded in August that children taking Effexor had 8.84 times the risk of suicidal behavior or thinking compared with children taking sugar pills.

British authorities warned physicians last year not to prescribe a range of antidepressants to children. The FDA has called for a more cautious interpretation of the data, which an agency advisory committee is expected to discuss at a meeting next week.

Yesterday's hearings, which included testimony from officials from seven pharmaceutical companies, grappled with ways to make negative study results about drugs more accessible to the public. Recent proposals by manufacturers, medical journal editors and members of Congress have called for various schemes for publicly registering all drug trials and, in some cases, disclosing the results.