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FDA under fire over barred antidepressant report

Scientist links antidepressants to suicide in kids

By Rob Waters
SPECIAL TO THE CHRONICLE

A scientist at the Food and Drug Administration has been barred from publicly presenting his finding that several leading antidepressants may increase the risk of suicidal behaviors among children, according to sources inside the FDA.

FDA medical officer Andrew Mosholder was to present his report Monday at an FDA advisory hearing in Washington that promises to be a contentious affair involving competing medical experts and parents whose children took their own lives while on the medications.

A senior FDA official said the study wouldn't be presented because it wasn't "finalized." But critics fear that the agency's action indicates it is not prepared to take stronger action against the drugs, despite warnings about their possible effects on children.

Mosholder had been asked by the agency to perform a safety analysis of antidepressants after reports emerged this summer of high rates of suicidal behavior among children enrolled in clinical trials for Paxil, Effexor and other antidepressants.

Mosholder, a child psychiatrist, reviewed data from 20 clinical trials involving more than 4,100 children and eight different antidepressants. His preliminary analysis, according to two FDA sources familiar with the report's contents, concluded that there was an increased risk of suicidal behavior among children being treated for depression with Paxil and several other antidepressants.

An initial agenda for Monday's hearing listed Mosholder and his findings, but his presentation was removed from a revised agenda, and Mosholder was told that he could not present his findings at the hearing, one FDA official, who wished to remain anonymous, told The Chronicle.

According to the official, in early January, Russell Katz, director of the division of neuropharmacological drug products, called Mosholder in for a meeting. "He told him that he was sorry, but he wasn't going to be able to present (his report) because he had reached a conclusion and therefore was biased," the official said.

Mosholder declined several requests to be interviewed and was not made available despite repeated requests to FDA's press office. Katz was unavailable to comment on the charges.

In a telephone interview Friday with The Chronicle, Anne Trontell, deputy director of the agency's Office of Drug Safety, who is Mosholder's direct supervisor, said the analysis would not be presented because it had not yet been approved within her office.

"The consult on that is not finalized. It's not a final document within the Office of Drug Safety," Trontell said.

However, Trontell said that at Monday's hearing, Mosholder would provide a rundown of reports of suicidal behavior received by the agency from doctors and other professionals.

While Mosholder's safety analysis report may eventually be completed and made public, some FDA insiders fear that withholding it from Monday's hearing indicates that the agency may be siding with the pharmaceutical industry in its long-running battle with critics of antidepressants.

"Why is the agency sitting on its hands and acting as if there isn't a risk when their own scientists have looked at the data and concluded that there is?" one FDA official remarked.

The use of antidepressants and other psychiatric medication among children has more than tripled in recent years and now approaches adult usage rates, according to a January 2003 study in the Archives of Pediatric and Adolescent Medicine. Study author Julie Zito, an associate professor of pharmacy and medicine at the University of Maryland, estimates that more than 1 million American children used antidepressants in 2000.

Advocates of the drugs argue that they are imperfect but necessary weapons against a rising tide of mental illness among children.

Last month, a task force of the American College of Neuropsychopharmacology released its own preliminary review of published studies on antidepressants and suicide and stated it found no statistically significant increase in suicide attempts among children taking the drugs.

"The most likely explanation for the episodes of attempted suicide while taking SSRIs (selective serotonin reuptake inhibitors) is the underlying depression, not the SSRIs," said Graham Emslie, a child psychiatrist and researcher at the University of Texas Southwestern Medical Center in Dallas.

But critics, including consumer advocates and mental health professionals contend, based on other studies, that the drugs are often ineffective and sometimes dangerous and that the FDA has failed to vigorously investigate the risks and protect children's safety.

"The FDA is shielding the industry," said Vera Sharav, president of the Alliance for Human Research Protection, a consumer advocacy group.

Mosholder's analysis appears to be similar to the conclusions reached by British regulators, who told doctors in December to stop prescribing Paxil, Zoloft, Effexor and three other antidepressants to children because of an apparent "increased rate of self-harm and suicidal thoughts."

British regulators took action against Paxil in early June after new data presented to U.S. and British authorities showed that children taking the drug were nearly three times as likely to consider or attempt suicide as children taking placebos.

Later that month, the FDA issued a similar warning, urging doctors not to prescribe Paxil to children and announced that it would conduct a detailed review of pediatric trials of Paxil. The review was subsequently broadened to include seven other antidepressants, including top sellers Prozac, Zoloft and Effexor.

In October, the agency wrote to physicians to "call to (their) attention" reports of suicide among children in antidepressant trials. The agency did not, however, urge doctors to stop prescribing the drugs.

Several current and former FDA staff members interviewed by The Chronicle said the dispute over Mosholder's report highlights a lack of assertiveness within the agency over safety issues. They spoke of a split between the Office of Drug Safety — Mosholder's office — and the FDA's drug-reviewing divisions.

As an example, they cite a hearing last March on a rheumatoid arthritis drug, Arava, which had generated numerous reports of adverse effects, including nine deaths, after being approved by the FDA.

Members of the Office of Drug Safety, who had prepared a 37-page safety report, were present at the hearing but were not allowed to speak. A representative of the FDA division that originally approved the drug, along with the pharmaceutical company that makes the drug, did most of the talking.

A documentary crew from the PBS series Frontline filmed the meeting and afterward, in the hallway, caught up with David Graham, a senior epidemiologist with the Office of Drug Safety. The producers had been denied previous requests to interview Graham, but the government scientist gave a brief interview without permission.

"We had a different perspective, and we really weren't given an opportunity to present our side of the story," Graham, on camera, told the producers. "And the people who did present, the reviewing division and the company, you know, they didn't see a problem. This was a very hostile process. And let's just leave it at that."

Paul Stolley, a professor and former chairman of the department of epidemiology at the University of Maryland, spent a sabbatical year as a senior consultant in the Office of Drug Safety in 2000 and 2001. While there, he recalls, he tussled with agency managers over the safety of Lotronex, a drug used to treat irritable bowel syndrome, a chronic but usually not serious disease.

Stolley said his investigation uncovered high rates of negative side effects, including a number of deaths, among patients using the drug and led the company to withdraw the drug from the market.

A few months later, over Stolley's objections, the agency allowed the drug back on the market with a "risk management" program aimed at educating patients and doctors about the drug's risks. Stolley said he was excluded from internal FDA meetings on the issue.

"I'm worried about the agency," he says. "I didn't expect people to think I was right just because I was very senior. What I did expect was a vigorous debate and instead of having a vigorous debate, they made a policy decision and then excluded me."

Rob Waters' article, "A Suicide Side Effect? What parents aren't being told about their kids' antidepressants," appeared in the Jan. 4 edition of The Chronicle Magazine. E-mail him at robw001@pacbell.net.