News

Secret US report surfaces on antidepressants in children

Jeanne Lenzer *New York*

Internal memos and a secret government report about the negative effects of antidepressants in children—suppressed by the US Food and Drug Administration—have surfaced publicly.

The Alliance for Human Research Protection, a national network dedicated to ensuring ethical standards in medical research, published the documents on 26 July.

The published documents confirm earlier news accounts that a government expert with the FDA's Office of Drug Safety, Dr Andrew Mosholder, found that children taking antidepressants were twice as likely to become suicidal as children taking placebo. He reportedly urged the agency to follow the lead of British health authorities by warning doctors that the risks of the newer antidepressants, except fluoxetine, might outweigh the benefits when used in children.

The leaked documents show his data and conclusions. The FDA has subsequently acknowledged to the *BMJ* that Dr Mosholder was prevented from presenting his report at an advisory committee meeting on 2 February and was told that if he was asked any questions during the meeting he could respond to queries only by using a prepared script approved by his supervisors.

Dr Mosholder had evaluated data from 22 studies using nine drugs in 4250 children and found that 74 of the 2298 children taking antidepressants had a "suicide related event" compared with 34 of the 1952 children taking placebos.

When questioned about the decision to suppress Dr Mosholder's report, Dr Robert Temple, associate director for medical policy in the FDA's drug evaluation centre, defended the agency's actions. "We thought the analysis was premature," he told the *BMJ*.

Both the raw data and Dr Mosholder's interpretation were "imperfect" said Dr Temple, adding that some of the behaviours labelled "suicidal" were highly suspect and could have been accidents, such as a child "who hit her head with her hand." FDA officials acknowledged, however, that some cases classified as "accidental injury" could be suicide related. Because of this, the FDA has contracted with Columbia University to further study and classify events that might be considered to be suicide related.

Some of these events, he added, such as superficial cutting, "might be due to anxiety" and not represent true suicidal intent.

Dr Thomas Laughren, the FDA's team leader for psychiatric drug products, told the *BMJ* that he had reported the relative risk ratios of all the drugs evaluated at the advisory meeting and that it was Dr Mosholder's conclusions, and not the data, that were withheld.

Responding to critics who say studies of antidepressants other than fluoxetine show little or no efficacy in children, Dr Temple said absence of proof should not be interpreted to mean the drugs are ineffective.

Dr Jerome Hoffman, an epidemiologist and professor of medicine at the University of California at Los Angeles, told the *BMJ* that the flip side of Dr Temple's claim that antidepressants in children could be lifesaving is that they could be life threatening—as suggested by Dr Mosholder's report.

"Most Americans undoubtedly believe that the FDA demands reasonable evidence that a drug is safe before it is allowed to be used," said Professor Hoffman. "But this episode suggests that they reject this 'precautionary principle' in favour of the idea that no drug is dangerous unless it is 'proven' to be so."

"The FDA… attempted to silence Dr Mosholder [but] repeatedly claimed to 'support his concern' for the safety of children," added Professor Hoffman, "but this apparently didn't extend to supporting his desire to express that concern publicly. That may be the most dangerous aspect of this entire affair."

The FDA has launched a criminal investigation to find out which employees leaked Dr Mosholder's report. Meanwhile the suppression of the report has triggered Congressional investigations by Senator Charles Grassley, who has interviewed employees in the agency's Office of Drug Safety, where Dr Mosholder worked. □

Germany sets up quality control institute for health care

Annette Tuffs *Heidelberg*

Germany's federal joint committee of doctors, health insurance companies, and patients (the Gemeinsame Bundesausschuss) has announced the foundation of a new, independent Institute for Quality and Economic Efficiency in Health Care—Germany's equivalent of England's National Institute for Clinical Excellence.

The main task of the new institute, which has a staff of about 30, is to research the latest medical knowledge on diagnostics and therapy of selected diseases and provide expertise on quality and economic efficiency.

The institute will also evaluate the evidence based guidelines of the most common diseases and prepare recommendations for setting up disease management programmes. In addition, the institute will evaluate the effectiveness of drug treatment and prepare information about the quality and efficiency of health care for the public.

Its first director is Professor Peter Sawicki, a physician and diabetes specialist who founded a private research institute, the Institute for Evidence-Based Medicine, in 2002 (*BMJ* 2004; 328:485).

The establishment of the Institute for Quality and Economic Efficiency in Health Care has already been criticised by doctors and the pharmaceutical industry. Doctors fear that they will be confronted with "cookery book medicine" and "patronising state medicine," which will abolish every chance of giving individual treatment. They welcome, however, more scientifically based advice on effective drug treatment. The drug industry is sceptical of yet another bureaucratic obstacle to the introduction of innovative drug treatment.

Professor Sawicki says that innovations are not necessarily always beneficial and have to be scientifically evaluated for their clinical and economic benefits. But he accepts that independent evaluation should be carried out immediately after a drug's approval. □