FDA PUBLIC HEALTH ADVISORY

October 27, 2003

Subject: REPORTS OF SUICIDALITY IN PEDIATRIC PATIENTS BEING TREATED WITH ANTIDEPRESSANT MEDICATIONS FOR MAJOR DEPRESSIVE DISORDER (MDD)

Dear Health Care Professional:

The Food and Drug Administration (FDA) would like to call your attention to reports of the occurrence of suicidality (both suicidal ideation and suicide attempts) in clinical trials for various antidepressant drugs in pediatric patients with major depressive disorder (MDD). While occurrences of suicidality are not unexpected in patients with MDD, preliminary data suggest an excess of such reports for patients assigned to several of these antidepressant drugs compared to those assigned to placebo. FDA has completed a preliminary review of such reports for 8 antidepressant drugs (citalopram, fluoxetine, fluvoxamine*, mirtazapine, nefazodone, paroxetine, sertraline, and venlafaxine) studied under the pediatric exclusivity provision, and has determined that additional data and analysis, and also a public discussion of available data, are needed. FDA plans to hold an advisory committee meeting before the Psychopharmacologic Drugs Advisory Committee and the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee on February 2, 2004.

You may also be aware of press and medical journal reports of suicide attempts and completed suicides in pediatric patients receiving antidepressants. Such reports are very difficult to interpret, in the absence of a control group, as these events also occur in untreated patients with depression. Data available to FDA on these spontaneous reports will also be presented at the February 2, 2004, advisory committee meeting mentioned above.

Pending the broad public discussion of these issues, FDA wishes to emphasize several critical points.

In the 20 placebo-controlled trials being considered for these 8 drugs, involving over 4100 pediatric patients, there have been no reports of completed suicides. However, FDA has not at this point been able to rule out an increased risk of suicidality for any of these drugs, including Paxil (paroxetine), which was the subject of a FDA Talk Paper on June 19, 2003.

FDA emphasizes that, for the 7 drugs evaluated in pediatric major depressive disorder (MDD), data reviewed by FDA were adequate to establish effectiveness in MDD for only one of these drugs, Prozac (fluoxetine). Failure to show effectiveness in any particular study in pediatric MDD, however, is not definitive evidence that the drug is not effective since trials may fail for

many reasons. FDA recognizes that pediatric MDD is a serious condition for which there are few established treatment options, and that clinicians often must make choices among treatments available for adult MDD.

FDA emphasizes that these drugs must be used with caution. Prescribers are reminded of the following statement present in all antidepressant labeling:

"Suicide: The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for Drug X should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose."

As recommended in the June 19, 2003 Talk Paper for Paxil, FDA advises that caretakers of pediatric patients receiving treatment with Paxil, or with any of the antidepressants, talk to their doctor regarding the use of the drug. **Patients should not discontinue use of any of these drugs without first consulting with their physicians, and, for certain of these drugs, it is important that they not be abruptly discontinued (see labeling for individual drugs).**

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*Although fluvoxamine data was reviewed with the other antidepressant drugs data, it should be noted that it is not approved as an antidepressant in the United States.

Additional Information (FDA Talk Paper)

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