Thomas Laughren, M.D.
Director, Division of Psychiatry Products
Food and Drug Administration / CDER
10903 New Hampshire Ave
WO Building 22, Room 4114
Silver Spring, MD 20993

14 April 2009

Re: **Seroquel for Adjunctive Therapy in Major Depressive Disorder**

Dear Dr. Laughren,

We applaud the recently announced recommendation of the Psychopharmacologic Drugs Advisory Committee which met April 8th in Silver Spring, that FDA "**not expand the label for Seroquel to include use as monotherapy**" in Major Depressive Disorder (MDD) or in Generalized Anxiety Disorder (GAD).

In a letter to you from Dr. Sidney Wolfe of *Public Citizen*, it is stated clearly that the reasons for PDAC's unanimous vote included, but were not limited to, concerns about the association of Seroquel use with "*(1) heavy sedation; (2) tardive dyskinesia – an irreversible, disabling movement disorder; and (3) metabolic derangements including weight gain, adverse effects on lipids, and hyperglycemia, all of which may confer cardiovascular risk.*" Furthermore, despite these adverse effects "***rampant off-label and inappropriate prescribing of Seroquel*** *and other atypical antipsychotics already occurs, especially in vulnerable populations*".

While I concur whole-heartedly with most of the PDAC committee's observations and recommendations, I feel obligated to take exception to a critical detail of the Committee's recent letter. With full due respect to the members of the PDAC, I believe that extension of Seroquel's approval to the narrow indication of ***"adjunctive therapy in MDD"***, even if accompanied by a boxed warning prohibiting Seroquel's use as monotherapy, will predictably result in exposure of many-fold thousands of patients with symptoms of depression to the medical and neurological risks associated with use of Seroquel without demonstrated or even likely benefit to justify those risks.

While most clinicians will agree that refractory depression, defined rigorously, is a serious clinical problem, the medical management of refractory depression must be approached with sober circumspection. Physicians and other qualified prescribers are already legally permitted to prescribe Seroquel and other atypical antipsychotics for adjunctive treatment of MDD. Furthermore, and most critically in the current climate of aggressive pharmaceutical product marketing, there is every reason to believe that the inherent ambiguity in the definition of "*adjunctive treatment of MDD*" will result in widespread promotion of the use of Seroquel for treatment of patients with garden variety depression in whom there is little or no proof of benefit from Seroquel or other atypical antidepressants.

In my opinion, and, I believe, in the opinion of clinicians and patient advocates with whom I am in frequent contact, for the FDA to extend labeling to adjunctive treatment of MDD would constitute *de facto* endorsement of a practice that is arguably **unjustified** on clinical grounds most of the time and certainly abusive from the standpoint of fiscal responsibility. We strongly urge you to heed the recommendations of the PDAC and not expand the label for Seroquel to include use as monotherapy in MDD or GAD. **We further urge that the FDA not grant labeling extension to adjunctive treatment of MDD**. It is both unnecessary and ill-advised for the reasons outlined above.

Sincerely and respectfully,

/s/

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cc: Sidney Wolfe, M.D.,
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