# Statement of Ken Duckworth, M.D.

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# Submitted to

# FDA Psychopharmacologic Drugs Advisory Committee

# Public Hearing on Suicidality & Adult Antidepressants

# December 1, 2006

This statement is offered on behalf of the National Alliance on Mental Illness (NAMI). As its Medical Director, I am board-certified in adult, child and forensic psychiatry. I am an Assistant Professor of Psychiatry at Harvard Medical School and have held many clinical positions. I also am Medical Director of Vinfen Corporation, a community-based human services agency in Cambridge, Massachusetts.

From 2000 to 2003, I served as state medical director and Acting Commissioner for the Massachusetts Department of Mental Health. I receive no consulting, speaking or advisory fees from any pharmaceutical company.

Founded in 1979, NAMI is the nation's largest, grassroots organization of consumers and families dedicated to improving the lives of people living with serious mental illness. Our interest in anti-depressants is saving lives.

**Hearing Timing Concern**

My understanding is that the Food & Drug Administration has conducted its own data review of clinical studies concerning antidepressants and potential links—risks—of suicide in adult patients.

The review has not been released publicly at the point in time that public comments are required to be filed (December 1) in advance of the hearing. Thus, organizations, outside experts, and individuals will not be able to address in advance specific findings of the FDA review.

The December 1st deadline coincides with the launch of the very first National Anti Stigma Campaign on Mental Health by the Department of Health & Human Services and the Ad Council—as part of the national suicide prevention strategy recommended by the Surgeon General in 1999 and the President's New Freedom Commission on Mental Health in 2003..

Ironically, headlines, lead paragraphs, and sound bites—rather than careful consideration of risks—have contributed to the stigmatization of one of the most effective, immediate treatment for major depression.

For example, prior to the Advisory Committee's review of suicidality concerns in 2004 related to the use of antidepressants with adolescents, media reports of possible action are considered to have initiated an at least 20% drop in prescriptions.

It is essential that no statement or decision of the Advisory Committee contribute to a new kind of stigma surrounding mental illness—and thereby undermine the newly-launched National Anti Stigma Campaign.

**Recent Research: 2006 and Beyond**

Over this last year, the National Institute of Mental Health has released findings from the largest clinical trial ever conducted for major depression—STAR*D which stands for Sequenced Treatment Alternatives to Relieve Depression. These findings must guide the Committee's recommendations.

STAR*D has found that almost 70% of patients are helped by one or more drugs. Approximately 40% achieve remission on the first drug and 30% on their second. On third and fourth trials, the rate is 14% and 13% respectively.

The average length of time to achieve remission is six weeks, with between five and six as the average number of doctor visits. Forty percent of patients who eventually became symptom-free required eight or more weeks of additional treatment. Almost all who became symptom-free continued treatment over eight weeks, many for 12 weeks.

Depression kills. Remission saves lives. Lessons learned from STAR*D include the fact that treatment is often progressive and incremental, and that it is important to select the best possible, most effective medication that fits the individual, right from the start.

The selection requires more than medication. It involves communication and expectations. In 2005, NAMI conducted a survey that complements some of the STAR*D findings.

- On average, the majority of consumers with depression tried four medications.
- A majority had experienced six or more episodes of depression in their lifetimes, but only a third ever had discussed the possibility of relapse with physicians.
- Less than 25% were aware of differences between full and partial remission.
- Only 25% received "talk therapy" or counseling.

These markers are all relevant to calculation of overall risk—based on a thorough understanding of clinical treatment. That's the real-life picture of a dynamic, flexible process.

Research is ongoing. Exactly one month ago (November 13), NIMH announced that it is funding five new research projects to shed better light on potential links between antidepressants and suicidality.

The new multi-year projects "will clarify the connection" NIMH Director Thomas Insel, M.D. said in the announcement. They are intended to help determine why and how medication may trigger suicidality in some people, but not others. They are needed as part of the overall effort to identify vulnerability factors. Please consider the dimensions of research that still remains. Keep in mind that taking regulatory action sometimes is easier than taking back a decision, even if conclusions based on new findings otherwise warrant.

**One Size Does Not Fit All; Not All Risks Are the Same**

One size does not fit all when it comes to treating mental illness. Sound clinical practice requires individualized treatment.

Medication is only one part of comprehensive, sound treatment strategy. Antidepressant response must be monitored in the short term, particularly when medications are switched or added. Hospitalization may be needed.

Multiple trials also may be needed before the right medication or dosage is found. It's the process, not the medication itself that may cause the risk of suicide to remain high. In addition, in the long-term, a combination of medication and psychotherapy is most effective for most people.

There is also a risk of an anti-depressant alone—without a mood stabilizer—"activating" a previously unknown vulnerability to bipolar illness. The risk is greater with patients who have bipolar illness in their family history.

There are strategies to mitigate this risk. It is one reason that careful monitoring is important in early stages of prescription. and that greater professional education of primary physicians, along with broader public and family education about bipolar illness is critically needed.

**The Problem of Causation**

Without the benefit of the FDA's review, we at least know that studies on the risk of suicide too often are short in duration and do not uniformly define suicidal behavior so as to ensure reliable results.

Interviews and self-reporting may be highly subjective or make only crude distinctions in ideation. Competing factors of causation may not be apparent or ever actually known. Here is one example:

A 2003 study on the relationship between antidepressants and suicide in children and adolescents found a correlation between increased the use of antidepressants and the decline of suicide rates between 1990 and 2000, within regional zip codes. That's good. At the same time, the highest rates of antidepressant use by zip codes coincided with the highest suicide rates. That seems bad; however, it also makes sense that the highest increase in use would occur in areas with the most depressed people and the highest suicide risk. It was an interesting study. But it did not tell us anything about any number of other possible causes—pro or con.

We do know that enormous barriers prevent adults from being treated.

Stigma is one of them, regardless of whether it attaches to the illness or the medication.

There also are discriminatory caps on mental health coverage; the shortage of mental health providers in many communities; a health care system that is fragmented and, lacks accountability, and that forces mental health professional to rush through sessions with patients.

NAMI consumers and families know about barriers. So do many others. The consequences for this broken system are dire. They contribute to the risk overall risk, and it must be include it in your calculation.

The FDA must not add to barriers. FDA's assessment of risk must consider the broader context in which people are discouraged from treatment.

Untreated depression is a public health crisis. That's why the Surgeon General and HHS are launching the National Anti-Stigma Campaign this month as part of a national suicide prevention strategy. There is a profound need for coordinated federal, state and local participation and coordination. FDA must be part of the solution.

**Suicide Risk & Black Box Warning**

The greatest risk of suicide is depression that goes untreated. Hesitation when clinical action is can result in suicide.

Benefits and risks must be considered simultaneously. Any action the FDA takes must take care to emphasize simultaneously the risk from depression that goes untreated or is inadequately addressed.

In October 2004, when FDA issued its requirement of a "black box warning" for the use of antidepressants for children and adolescents, NAMI's major criticism was the failure to acknowledge within the warning that untreated depression is directly linked to suicide and that antidepressant medications are effective in treatment.

NAMI supports efforts to ensure that all data concerning the impact of antidepressants is made available to the public and independent researchers in order to better inform physician and patient decisions. In our 2004 testimony, NAMI called for public access to the complete results of all clinical and controlled trials—regardless of the trial sponsor and outcome.

**Other NAMI Submissions**

For the record, NAMI also is submitting separately copies of three brochures developed in partnership with the Suicide Prevention Resource and Education Development Center, funded by the federal Substance Abuse & Mental Health Services Administration (SAMHSA). The guides help bridge a gap by focusing specifically on treatment of suicide attempts—targeted to hospital emergency professionals, survivors, and family members. Their purpose is to help reduce the risk of additional attempts.

Keep in mind that an estimated 30-50% of individuals who die from suicide have made previous attempts. That must be part of your consideration.

I also direct you to the statement submitted in advance by Bob Carolla, NAMI's director of media relations, who is scheduled to testify in person on December 13th. He is a consumer who confronted major depression in the early 1980s before antidepressants were available and then again ten years ago. His "before and after" perspective on the use of antidepressants and suicidality issues is very relevant for your deliberations.

**Conclusion**

In summary:

- FDA policy must include appreciation of the broader national suicide prevention strategy, and concern for stigmatization of treatment options and other barriers to treatment.
- There should be public access to complete results of all clinical and controlled trials regardless of the trial sponsor and outcome, in order to fully inform treatment decisions.
- If a black-box warning for adults is adopted, we need to learn from the unintended consequences of the warning imposed for children and adolescents. It should acknowledge clearly that untreated depression is directly linked to suicide and that antidepressant medications are effective in treatment. Traditionally, FDA has not included such an approach in its regulation, but a more holistic, balanced perspective on benefits and risks is needed.

- Broader education of primary physicians and families about the risk of bipolar factors in using antidepressants is needed, including monitoring protocols.

For further information about NAMI's position on this issue or to learn more about NAMI, please contact NAMI's Director of Policy & Legal Affairs, Ron Honberg at 703-524-7600 by asking for Laura Usher.

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