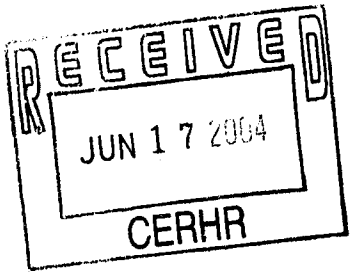

June 17, 2004

Dr. Michael Shelby, Director
Center for the Evaluation of Risks to Human Reproduction
National Toxicology Program
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Via electronic mail to shelby@niehs.nih.gov and fax to 919-316-4511

Dear Dr. Shelby:

I am writing in response to the National Toxicology Program's notice on the Expert Panel Report regarding questions on the reproductive and developmental toxicity of fluoxetine (Prozac). The action taken (e.g., convening the expert panel) thus far is puzzling and certainly is in conflict with the approval for use of this drug in younger populations and in premenstrual dysphoric disorder by the very agency—the Food and Drug Administration—whose mission it is to determine drug safety. This smacks of redundancy and waste of federal resources. But what is most outrageous is the lack of proper research perspective on the part of the panel.

The panel report acknowledges that tens of thousands of persons over the entire age span have been treated with fluoxetine for years, yet does not understand that it is the human outcomes data that should be the focus of any further inquiry—NOT basic dosing experiments on nonhuman animals.

As an epidemiologist, I can vouch for the vast superiority of data on reproductive outcomes and development collected from humans under realistic dosages and in the diverse milieu of everyday life. The latter includes variation in body weight and fat distribution, other drugs, smoking, sleep duration, family history, health care access, comorbidity, and other exposures. These are extremely important modifiers of the outcomes in question and can never be accounted for in laboratory experiments on nonhuman species living in situations far from human conditions. The basic laboratory toxicology data so collected on nonhuman species can never be generalized, even remotely, to answering the questions being asked regarding the safety of fluoxetine in younger ages and women of child bearing years. We are all too aware of the errors that have been made in the past in extrapolating safety from narrow high dose experiments on nonhuman animals to pregnant women, for example.

Most importantly, we are indeed fortunate to have the truly relevant data (or the means to easily obtain it) at hand in this particular case. In addition to already collected data and ongoing studies on fluoxetine, long term follow-up on thousands of persons who participated in previous trials can be carried out quickly. Furthermore, nested case-control and historical cohort studies could be performed on the numerous ongoing population-based cohorts, many of which include random samples of children being followed, with data being used to address many epidemiological questions. Indeed, at present I am aware of several ongoing clinical trials of

fluoxetine in children and adolescents, and there are abundant data sets on women that include pregnancies over the course of observation.

I am appalled that, if the panel's recommendations are accepted, the millions of NIH taxpayer dollars that have gone into collecting priceless, relevant human data that could truly address the questions about fluoxetine would go to waste, and virtually useless (dangerously so) data will be collected in painful experiments on nonhuman animals (most likely rats, dogs and primates). Something in the scientific and regulatory process has gone badly awry here, with one government agency (NTP) apparently duplicating the mission of another federal agency (that of the FDA).

If allowed to proceed, we will all suffer the consequences of bad data and wasted research dollars, and many animals will suffer being subjected to useless, painful, and deadly experimentation.

Sincerely,