DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

August 17, 2004

Dear Psychopharmacologic Drugs Advisory Committee Members/Consultants
and Pediatric Advisory Committee Consultants:

I hope you all are well and are having a pleasant summer.

With this letter, I am forwarding the background package containing materials for the September 13-14, 2004, Advisory Committee meeting. As a reminder, the meeting is taking place on **Monday, September 13 and Tuesday, September 14.** We are scheduled to begin the discussions on Monday at 8:00 a.m. We are planning on ending at 6:30 p.m. On Tuesday, we are planning to begin discussions at 8:00 a.m. and end at approximately 5:00 p.m. The meeting will take place at the **Holiday Inn**, in Bethesda, Maryland located at 8120 Wisconsin Avenue (telephone number: 301-652-2000).

Included in this package are the following materials:

1. Attachment to this letter: Original Federal Register Notice for the meeting and the Amended Federal Register Notice;
2. Agency's background package:
   - An August 17, 2004 Memorandum;
   - A January 5, 2004 memo written by Dr. Thomas Laughren, M.D. , Team Leader, Division of Neuropharmacological Drug Products (DNDP) in preparation for the February 2, 2004 Advisory Committee meeting. This memo provides a more complete discussion of various events leading up to that earlier meeting and the basis for DNDP's analysis of the suicidality data. It also includes a summary of efficacy findings from the 15 studies in pediatric major depressive disorder (pp. 5-6 and Appendix 1);
   - Summary Minutes from the February 2, 2004, Advisory Committee;
   - Several published epidemiological studies that are pertinent to the concerns about suicidality in association with antidepressant drug treatment;
   - A recent paper (August 18, 2004) from JAMA providing the results of the Treatment for Adolescents with Depression Study (TADS), along with an editorial commenting on the findings from this trial;
   - A review by Dr. Greg Dubitsky from DNDP, providing details about the structure and conduct of these trials, and about the populations studied;
   - A review by Dr. Solomon Iyasu from Office of Counter-Terrorism and Pediatric Drug Development (OCTAP), describing the methods and results of OCTAP's independent appraisal of the Columbia classification effort. His review includes as appendices several documents from the Columbia University suicidality group describing their approach to the blinded classification of suicidality events;

- A review by Dr. Tarek Hammad from DNDP, providing the detailed results of the analysis of the pediatric suicidality data;
- A review by Dr. Andrew Mosholder from Office of Drug Safety (ODS), providing the results of his analysis of the of the original pediatric suicidality data completed before the results of the classification of cases was available, along with an update on that review to provide a comparison of the findings of that initial analysis with analyses conducted on the basis of the definitively classified cases.
- Public Health Advisories on suicidality and antidepressant medications issued by FDA on June 19, 2003, October 27, 2003, and March 22, 2004, and related documents.
- Product labeling for 10 antidepressants that have implemented the labeling changes announced in the March 22, 2004 Public Health Advisory; and

3. Sponsor Briefing Packages
   - Eli Lilly and Company
   - Pfizer Incorporated

And finally, you have already received your travel information for both transportation and hotel. If by chance you have not received these documents, please contact me **immediately**.

Please feel free to contact me with any questions or issues regarding the meeting. I can be reached at: (301) 827-6790 or PatelA@cder.fda.gov.

I look forward to meeting you all in September and to some very interesting discussions.

Sincerely,

Anuja M. Patel, M.P.H
Executive Secretary,
Advisors and Consultants Staff
Center for Drug Evaluation and Research (CDER), FDA
(301) 827-6790
(301) 827-6776 (FAX)
Email: PatelA@cder.fda.gov

Attachment
Enclosures

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2004N-0330]

Pediatric Ethics Subcommittee of the Pediatric Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of the Pediatric Ethics Subcommittee of the Pediatric Advisory Committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Pediatric Ethics Subcommittee of the Pediatric Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the Pediatric Advisory Committee on FDA's and certain Department of Health and Human Services' (HHS) regulatory issues.

Date and Time: The meeting will be held on September 10, 2004, from 8:30 a.m. to 3:30 p.m.

Addresses: Electronic copies of the documents for public review can be viewed at the Pediatric Advisory Committee (PAC) docket site at *http://www.fda.gov/ohrms/dockets/ac/acmenu.htm*. (Click on the year 2004 and scroll down to PAC meetings.) Electronic comments should be submitted to *http://www.fda.gov/dockets/ecomments*. Select Docket Number 2004N-0337, entitled "Subpart D IRB Referral" and follow the prompts to submit your statement. Written comments should be submitted to Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Received comments may be viewed on the FDA Web site at: *http://www.fda.gov/ohrms/dockets/dockets/04n0337/04n0337.htm* or may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Location: Regency Room, DoubleTree Hotel, 1750 Rockville Pike, Rockville, MD.

Contact Person: Jan N. Johannessen, Office of the Commissioner (HF-33), Food and Drug Administration, 5600 Fishers Lane (for express delivery, rm 17-51), Rockville, MD 20857, 301-827-6687, or by e-mail: *jjohannessen@oc.fda.gov*. Please call the FDA Advisory Information Line, 1-800-741-8138 (301-443-0572 in the Washington, DC area), code 8732310001, for up-to-date information on this meeting.

Agenda: On Friday, September 10, 2004, the Pediatric Ethics Subcommittee of the Pediatric Advisory Committee will meet to discuss a referral by an Institution Review Board (IRB) of a proposed clinical investigation that involves both an FDA-regulated product and research involving children as subjects that is conducted or supported by HHS. The proposed clinical investigation is entitled "Effects of a Single Dose of Dextroamphetamine in Attention Deficit Hyperactivity Disorder (ADHD): A Functional Magnetic Resonance Study." Because the proposed clinical investigation would be regulated by FDA, and conducted or supported by HHS, both FDA and the Office for Human Research Protections, HHS, will participate in the meeting.

After presentation of an overview of the IRB referral process, background information on the ADHD, an overview of the protocol and the referring IRB's deliberations on the protocol, and a summary of public comments received concerning whether the protocol should proceed, the subcommittee will discuss the proposed protocol and develop a recommendation regarding whether the protocol should proceed. The subcommittee's recommendation will then be presented to the FDA Pediatric Advisory Committee on September 15, 2004; the announcement of the September 15, 2004, meeting can be found elsewhere in this issue of the **Federal Register**.

Also elsewhere in this issue of the **Federal Register** is a document announcing a public comment period concerning whether the proposed clinical investigation should proceed. Information regarding submitting comments during that period is contained in that document.

The background materials for the subcommittee meeting will be made publicly available no later than the day before the meeting and will be posted under the Pediatric Advisory Committee (PAC) Docket site at *http://www.fda.gov/ohrms/dockets/ac/acmenu.htm*. (Click on the year 2004 and scroll down to PAC meetings.)

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the subcommittee. Written submissions may be made to the contact person by August 25, 2004. Oral presentations from the public will be scheduled between approximately 11 a.m. and 12 noon.

Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person by August 25, 2004, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Persons attending FDA's advisory committee meetings are advised that the agency is not responsible for providing access to electrical outlets.

FDA welcomes the attendance of the public at its advisory committee meetings and will make every effort to accommodate persons with physical disabilities or special needs. If you require special accommodations due to a disability, please notify Jan Johannessen at least 7 days prior to the meeting.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: July 29, 2004.

William K. Hubbard,

Associate Commissioner for Policy and Planning.

[FR Doc. 04-17824 Filed 7-30-04; 3:42 pm]

BILLING CODE 4160-01-S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

[Docket No. 2004N-0330]

Food and Drug Administration

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committees: Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee.

General Function of the Committees: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on September 13, 2004, from 8 a.m. to 6:30 p.m. and on September 14, 2004, from 8 a.m. to 5 p.m.

Addresses: Electronic comments should be submitted to *http://www.fda.gov/dockets/ecomments*. Select "2004N-0330—Suicidality in

Clinical Trials for Antidepressant Drugs in Pediatric Patients'' and follow the prompts to submit your statement. Written comments should be submitted to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5600 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments received by August 23, 2004, will be provided to the committee before the meeting. Comments received after August 23, 2004, will be reviewed by FDA's decision makers.

Location: Holiday Inn, Versailles Ballrooms, 8120 Wisconsin Ave., Bethesda, MD.

Contact Person: Anuja Patel, Center for Drug Evaluation and Research (HFD–21), Food and Drug Administration, 5600 Fishers Lane (for express delivery, 5630 Fishers Lane, rm. 1093), Rockville, MD 20857, 301–827–7001, FAX: 301–827–6776, e-mail: *patelA@cder.fda.gov*, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area), code 3014512544. Please call the Information Line for up-to-date information on this meeting.

Agenda: The Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee will discuss 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 and other psychiatric disorders. Preliminary risk data based on the classification of these adverse event reports by the pharmaceutical sponsors of these products were presented at the joint meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee held on February 2, 2004. Since that meeting, experts in pediatric suicidality, assembled by Columbia University, have independently classified these reported events, and FDA has conducted an analysis of these data. On September 13 and 14, 2004, the committees will consider the results of FDA's analysis of these independently classified events and will consider what further regulatory action may be needed with regard to the clinical use of these products in pediatric patients. The committees will also consider further research needs to address questions on this topic.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the Division of Dockets Management before August 23, 2004, as previously stated (see *Addresses*). Oral presentations from the public will be scheduled between approximately 2 p.m. to 6 p.m. on September 13, 2004. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before August 27, 2004, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Persons attending FDA's advisory committee meetings are advised that the agency is not responsible for providing access to electrical outlets.

FDA welcomes the attendance of the public at its advisory committee meetings and will make every effort to accommodate persons with physical disabilities or special needs. If you require special accommodations due to a disability, please contact Anuja Patel at 301–827–7001, at least 7 days in advance of the meeting.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: July 29, 2004.

William K. Hubbard,

Associate Commissioner for Policy and Planning.

[FR Doc. 04–17822 Filed 7–30–04; 3:41 pm]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Public Health and Science and Food and Drug Administration

[Docket No. 2004N–0337]

Solicitation of Public Review and Comment on Research Protocol: Effects of a Single Dose of Dextroamphetamine in Attention Deficit Hyperactivity Disorder; A Functional Magnetic Resonance Study

AGENCY: Office of Public Health and Science and Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Office for Human Research Protections (OHRP), Office of Public Health and Science, Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA), HHS are soliciting public review and comment on a proposed research protocol entitled ''Effects of a Single Dose of Dextroamphetamine in Attention Deficit Hyperactivity Disorder (ADHD); A Functional Magnetic Resonance Study.'' The proposed research would be conducted at the National Institutes of Health (NIH) and supported by NIH's National Institute of Mental Health (NIMH). Public review and comment are solicited regarding the proposed research protocol under the requirements of HHS and FDA regulations.

DATES: To be considered, written or electronic comments on the proposed research must be received on or before 4:30 p.m. on August 20, 2004.

ADDRESSES: Electronic copies of the documents for public review can be viewed at the Pediatric Advisory Committee (PAC) Docket site at *http://www.fda.gov/ohrms/dockets/ac/acmenu.htm*. (Click on the year 2004 and scroll down to PAC meetings.) Submit written comments to the Division of Dockets Management (HFA–305), Docket No. 2004N–0337, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. All comments should be identified with the docket number found in brackets in the heading of this document. Received comments may be viewed on the FDA Web site at: *http://www.fda.gov/ohrms/dockets/dockets/04n0337/04n0337.htm*, or may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Julia Gorey, Office for Human Research Protections, The Tower Building, 1101 Wootton Pkwy., suite 200, Rockville, MD 20852, 301–496–7005, FAX: 301–402–2071, e-mail: *Jgorey@osophs.dhhs.gov*; or Jan N. Johannessen, Office of the Commissioner (HF–33), Food and Drug Administration, 5600 Fishers Lane (for express delivery, rm. 17–51), Rockville, MD 20857, 301–827–3340, or by e-mail: *jjohannessen@fda.gov*.

SUPPLEMENTARY INFORMATION: All studies conducted or supported by HHS which are not otherwise exempt and which propose to involve children as subjects require Institutional Review Board (IRB) review in accordance with the provisions of HHS regulations for the protection of human subjects at 45 CFR part 46, subpart D. Under FDA's interim final rule effective April 30, 2001 (21 CFR part 50, subpart D), FDA adopted similar regulations to provide safeguards for children enrolled in clinical investigations of FDA-regulated products. Because the proposed research, ''Effects of a Single Dose of Dextroamphetamine in Attention Deficit Hyperactivity Disorder; A Functional Magnetic Resonance Study,'' would be

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Joint meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee; Amendment of Notice

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

The Food and Drug Administration (FDA) is announcing an amendment to the notice of the meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee. This meeting was announced in the Federal Register of August 4, 2004 (69 FR 47157-47158). The amendment is being made to reflect changes in the Addresses and Procedure portions of the document. There are no other changes.

FOR FURTHER INFORMATION CONTACT: Anuja Patel, Center for Drug Evaluation and Research (HFD-21), Food and Drug Administration, 5600 Fishers Lane (for express delivery, 5630 Fishers Lane, Rm. 1093) Rockville, MD 20857, 301/827-7001, Fax: 301/827- 6776 or email: patelA@cder.fda.gov.

SUPPLEMENTARY INFORMATION: In the Federal Register of August 4, 2004, FDA announced that a meeting of the Psychopharmacologic Drugs Advisory Committee and the Pediatric Advisory Committee will be held on September 13 and 14, 2004. On page 47157, in the third column, the Addresses and Procedures portions of the meeting are amended to read as follows:

Addresses: Electronic comments should be submitted to http://www.fda.gov/dockets/ecomments. Select "2004N-0330-- Suicidality in Clinical Trials for Antidepressant Drugs in Pediatric Patients" and follow the prompts to submit your statement. Written comments should be submitted to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, Maryland 20852. Comments received by August 23, 2004, will be provided to the committee prior to the meeting. Comments received after August 23, 2004, will be reviewed by the FDA decision-makers.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the Division of Dockets Management, as stated above in the Addresses section. Oral presentations from the public will be scheduled between approximately 2 p.m. to 6 p.m. on September 13, 2004. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before August 27, 2004, 4:30 p.m. EST and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation. Docket "2004N-0330-- Suicidality in Clinical Trials for Antidepressant Drugs in Pediatric Patients" will remain open for public submissions until July 29, 2005.

This notice is given under the Federal Advisory Committee Act (5 U.S.C. app. 2 and 21 CFR Part 14, relating to advisory committees.

Dated: August 16, 2004

Anuja M. Patel, M.P.H.
Executive Secretary, PDAC

Dated: 8/17/04

for
Karen Templeton-Somers, Ph.D.
Team Leader