



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmaceutical Science/Immediate Office

Memorandum

Date: October 22, 2007

From: Raanan A. Bloom, Ph.D.
OPS/IO/PARS

To: Scott N. Goldie
OPS/ONDQA/DPMA

Through: Jon Clark, M.S.
OPS/IO/PARS

Subject: Zyprexa® Adhera™ (Olanzapine long-acting injection)
Request for Categorical Exclusion

NDA 022-173
Submission Date: April 27, 2007

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Background

Eli Lilly and Company has filed a new drug application, NDA 22-173, to gain approval for Zyprexa® Adhera™ (Olanzapine Pamoate Depot long-lasting injection), a psychotropic agent belonging to the thienobenzodiazepine class indicated for treatment of schizophrenia.

Pursuant to 21 CFR 25.31(b) (Environmental Impact), Eli Lilly has claimed a categorical exclusion for the present application based on the expected introduction concentration of less than 1 µg/L. In addition, as required under 21CFR25.15(d), Lilly states that there are no known “extraordinary circumstances” for the proposed action.

Review of the Current Submission

An Environmental Assessment (EA) was previously submitted by Eli Lilly for olanzapine (NDA 20-592; September 21, 1995). A FONSI was granted on August 2, 1996. With approval of the present NDA, Eli Lilly projects the US annual peak sales volume of

olanzapine to be below (b) (4). Assuming a daily discharge of 1.214×10^{11} liters water from sewage treatment facilities in the United States, an EIC of (b) (4) (ppb) is estimated. This value meet the concentration-based categorical exclusion criteria of 1 µg/L as stated at 21CFR25.31(b).

Our evaluation of the submitted information and available ecotoxicity data (see below) provides no reason to differ with Eli Lilly's statement that "there are no extraordinary circumstances for this proposed action."

Ecotoxicity Data: Olanzapine

Rainbow trout 96-hour median lethal concentration: 1.74 mg/L.

Daphnia magna 48-hour median effective concentration: 8.0 mg/L.

Green algae (*S. capricornutum*) median effective concentration: >14.1 mg/L (average specific growth rate).

Microorganisms:

fungus (*Chaetomium globosum*): MIC = 400 mg/L

mold (*Aspergillus flavus*): MIC = 1000 mg/L

soil bacteria (*Comamonas acidovorans*): MIC > 1000 mg/L

N-fixing bacteria (*Azotobacter chroococcum*): MIC > 1000 mg/L

blue-green algae (*Nostoc* sp.): MIC = 255 mg/L

Source: http://ehs.lilly.com/msds/msds_olanzapine_for_injection.html and 9/21/05 EA

Comments and Conclusions

Based on an evaluation of the provided information, this application qualifies for a categorical exclusion under 21 CFR 25.31 (b).

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Raanan Bloom
10/22/2007 03:39:45 PM
ENV ASSESSMENT

Jon E. Clark
10/23/2007 11:09:01 AM
CHEMIST

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD- 420 Division of Medication Errors and Technical Support (DMETS) Attention: Angela Robinson		FROM: HFD-130 / Division of Psychiatry Products Keith Kiedrow, Regulatory Project Manager		
DATE October 2, 2007	IND NO.	NDA NO. 22-117	TYPE OF DOCUMENT tradename review request	DATE OF DOCUMENT September 25, 2007
NAME OF DRUG RELPREV (Zypexa long acting injection)	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG Schizophrenia	DESIRED COMPLETION DATE December 1, 2007	
NAME OF FIRM: Eli Lilly				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Attached is a request for trademark review by Lilly for NDA 22-173, Zypexa RELPREV. Please review the attached submission with regard to the tradename. Please also continue to review (reference the prior consult sent May 16, 2007), the packaging/carton labeling found in the following edr link – \ICDSESUB1\NONECTD\N22173\N_000\2007-4-30. Thanks!				
SIGNATURE OF REQUESTER LCDR Keith Kiedrow, Pharm.D. Regulatory Project Manager 301-796-1924 keith.kiedrow@fda.hhs.gov		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

September 25, 2007

**Request for TRADEMARK Review:
FDA response Requested**

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

**Re: IND 60,701: Olanzapine long-acting injection (LY170053); Serial No. 170
Request for TRADEMARK Review**

Dear Dr. Laughren:

Reference is made to IND 60,701 for Olanzapine Long Acting Injection and to our NDA 22-173, submitted under Section 505 (i) of the Federal Food, Drug, and Cosmetic Act and the NDA dated April 27, 2007, received April 30, 2007, under Section 505 (b) of the Federal Food, Drug, and Cosmetic Act.

Additional reference is made to the amendment dated March 30, 2007 (serial #152) to IND 60,701 containing Lilly's request for an evaluation of the trademark ZYPREXA ADHERA and the response from FDA dated May 24, 2007, which conveyed Division of Drug Marketing, Advertising, and Communications (DDMAC) objections to the trademark ZYPREXA ADHERA. Lastly, reference is made to Lilly's June 30, 2007 rebuttal (serial #160) to DDMAC's objections and the secure email response dated August 30, 2007 from Dr. Keith Kiedrow of FDA's Division of Psychiatry Products which reaffirmed DDMAC's objections to the use of the trademark ZYPREXA ADHERA.

Eli Lilly and Company has completed an internal and external assessment of additional possible proprietary trademarks for olanzapine long-acting injection. Based on the results of this global evaluation, we propose ZYPREXA RELPREV as the trademark and hereby request a trademark evaluation by the Division of Drug Marketing, Advertising, and Communications (DDMAC) and the Division of Medication Errors and Technical Support (DMETS).

Lilly conducted a search of the United States Trademark office records for ZYPREXA RELPREV and filed an application for trademark registration in the U.S. on August 23, 2005. The trademark was examined by the U.S. Trademark office and accepted by the

trademark examiner. It subsequently was published for opposition on May 1, 2007, without objection, and was issued a Notice of Allowance on July 24, 2007.

In addition to the extensive legal review of ZYPREXA RELPREV, the trademark was evaluated for safety by Med-E.R.R.S., a subsidiary of the Institute for Safe Medication Practices (ISMP) using prescription simulation, expert panel review and the ERRS MODELTM of analysis, which is a modification of the Failure Mode and Effects Analysis (FMEA)¹. FMEA is a technique used to uncover design flaws or other product defects in such a way that may predict and limit the consequences of human error. The FMEA process considers the environment and conditions under which the product will be used and identifies potential problems arising from look-alike, sound-alike, and other types of nomenclature problems. As such, the ERRS MODELTM brings to light potential problems related to the safe use of proposed product trademarks.

The overall conclusion from the U.S. Med-E.R.R.S. evaluation is that Lilly's ZYPREXA RELPREV trademark is acceptable from a safety standpoint. The evaluation did note slight look-alike similarity between the suffix RELPREV and RELPAX (eletriptan; used in the treatment of migraines). RELPAX is an oral tablet with a different indication for use than ZYPREXA RELPREV. There are no overlapping dosage strengths or administration frequencies.

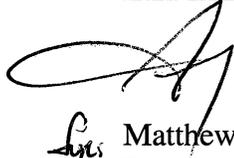
Therefore, we respectfully request that you consider the appropriateness of ZYPREXA RELPREV. Based on the NDA review timeline, Lilly would like to request an expedited review of the trademark if possible.

Please be advised that the above referenced submission has been submitted to IND 60,701. We hereby request that the said submission be incorporated into the above listed NDA 22-173 by reference.

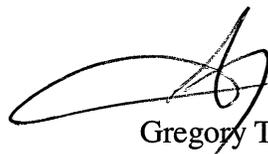
Please call me at (317) 433-1766 if you require any additional information or if there are any questions. Alternatively, you may contact Dr. Gregory T. Brophy, Director, U.S. Regulatory Affairs, at (317) 277-3799.

Sincerely,

ELI LILLY AND COMPANY



lrs Matthew R. Kuntz, R.Ph., M.B.A.
Regulatory Scientist
U.S. Regulatory Affairs



Gregory T. Brophy, Ph.D.
Director
U.S. Regulatory Affairs

¹ Cohen MR, Senders J, Davis NM. Failure Mode and Effects Analysis: A Novel Approach to Avoiding Dangerous Medication Errors and Accidents. *Hospital Pharmacy* 1994: 319-324, 326-328, 330.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0430.
Expiration Date: April 30, 2009
See OMB Statement on Reverse.

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR		2. DATE OF SUBMISSION 9/25/07	
3. ADDRESS (Number, Street, City, State and Zip Code) Lilly Corporate Center Indianapolis, IN 46285		4. TELEPHONE NUMBER (Include Area Code) (317) 276-2000	
5. NAME(S) OF DRUG (Include all available names: Trade, Generic, Chemical, Code) Olanzapine Pamoate Monohydrate Depot Formulation, (LY170053 Monohydrate Salt)		6. IND NUMBER (If previously assigned) 60,701	
7. INDICATION(S) (Covered by this submission) Schizophrenia			
8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED: <input type="checkbox"/> PHASE 1 <input type="checkbox"/> PHASE 2 <input type="checkbox"/> PHASE 3 <input type="checkbox"/> OTHER <u>NA</u> (Specify)			
9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS (21 CFR Part 314), DRUG MASTER FILES (21 CFR Part 314.420), AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.			
10. IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.			SERIAL NUMBER <u>0</u> <u>1</u> <u>7</u> <u>0</u>
11. THIS SUBMISSION CONTAINS THE FOLLOWING: (Check all that apply)			
<input type="checkbox"/> INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)		<input type="checkbox"/> RESPONSE TO CLINICAL HOLD	
PROTOCOL AMENDMENT(S):	INFORMATION AMENDMENT(S):	IND SAFETY REPORT(S):	
<input type="checkbox"/> NEW PROTOCOL	<input type="checkbox"/> CHEMISTRY/MICROBIOLOGY	<input type="checkbox"/> INITIAL WRITTEN REPORT	
<input type="checkbox"/> CHANGE IN PROTOCOL	<input type="checkbox"/> PHARMACOLOGY/TOXICOLOGY	<input type="checkbox"/> FOLLOW-UP TO A WRITTEN REPORT	
<input type="checkbox"/> NEW INVESTIGATOR	<input type="checkbox"/> CLINICAL		
<input type="checkbox"/> RESPONSE TO FDA REQUEST FOR INFORMATION	<input type="checkbox"/> ANNUAL REPORT	<input type="checkbox"/> GENERAL CORRESPONDENCE	
<input type="checkbox"/> REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED	<input checked="" type="checkbox"/> OTHER <u>Trademark Review</u>	(Specify)	
CHECK ONLY IF APPLICABLE			
JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.			
<input type="checkbox"/> TREATMENT IND 21 CFR 312.35(b)	<input type="checkbox"/> TREATMENT PROTOCOL 21 CFR 312.35(a)	<input type="checkbox"/> CHARGE REQUEST/NOTIFICATION 21 CFR 312.7(d)	
FOR FDA USE ONLY			
CDR/DBIND/DGD RECEIPT STAMP	DDR RECEIPT STAMP	DIVISION ASSIGNMENT:	
		IND NUMBER ASSIGNED:	

12.

CONTENTS OF APPLICATIONThis application contains the following items: *(Check all that apply)*

1. Form FDA 1571 [21 CFR 312.23(a)(1)]
2. Table of Contents [21 CFR 312.23(a)(2)]
3. Introductory statement [21 CFR 312.23(a)(3)]
4. General Investigational plan [21 CFR 312.23(a)(3)]
5. Investigator's brochure [21 CFR 312.23(a)(5)]
6. Protocol(s) [21 CFR 312.23(a)(6)]
- a. Study protocol(s) [21 CFR 312.23(a)(6)]
- b. Investigator data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
- c. Facilities data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
- d. Institutional Review Board data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
7. Chemistry, manufacturing, and control data [21 CFR 312.23(a)(7)]
- Environmental assessment or claim for exclusion [21 CFR 312.23(a)(7)(iv)(e)]
8. Pharmacology and toxicology data [21 CFR 312.23(a)(8)]
9. Previous human experience [21 CFR 312.23(a)(9)]
10. Additional information [21 CFR 312.23(a)(10)]

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? YES NOIF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? YES NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

Dr. Sara Corya
Medical Director-Zyprexa

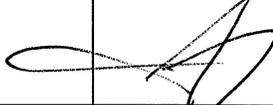
5. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set forth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

Gregory T. Brophy, Ph.D.
Director
US Regulatory Affairs

17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE



18. ADDRESS (Number, Street, City, State and Zip Code)

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

19. TELEPHONE NUMBER (Include Area Code)

(317) 277-3799

20. DATE

9/25/07

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
.901-B Ammendale Road
Beltville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please DO NOT RETURN this application to this address.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thomas Laughren
10/2/2007 12:56:58 PM

2 pages of Name Reveiw has been withheld
in full immediately following this page as B4
CCI/TS

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD- 420 Division of Medication Errors and Technical Support (DMETS) Attention: Angela Robinson		FROM: HFD-130 / Division of Psychiatry Products Keith Kiedrow, Regulatory Project Manager		
DATE July 18, 2007	IND NO. 60,701 N160	NDA NO. 22-173 letter date June 26, 2007	TYPE OF DOCUMENT tradename review request – rebuttal by sponsor to issued letter	DATE OF DOCUMENT June 26, 2007
NAME OF DRUG Zyprexa Adhera (olanzapine long acting injection)		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG Schizophrenia	DESIRED COMPLETION DATE August 31, 2007
NAME OF FIRM: Lilly				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
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V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Attached is a rebuttal from Lilly to the letter we (DPP) issued to the sponsor regarding their initial tradename, Adhera, for Zyprexa Long Acting Injection. I've also attached the letter that was issued. Please review and provide comments regarding the validity of their arguments. Thanks!				
SIGNATURE OF REQUESTER LCDR Keith Kiedrow, Pharm.D. Regulatory Project Manager 301-796-1924 keith.kiedrow@fda.hhs.gov		METHOD OF DELIVERY (Check one) x MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0430.
Expiration Date: April 30, 2009
See OMB Statement on Reverse.

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR ELI LILLY AND COMPANY	2. DATE OF SUBMISSION 6/26/07
3. ADDRESS (Number, Street, City, State and Zip Code) Lilly Corporate Center Indianapolis, IN 46285	4. TELEPHONE NUMBER (Include Area Code) (317) 276-2000
5. NAME(S) OF DRUG (Include all available names: Trade, Generic, Chemical, Code) Olanzapine Pamoate Monohydrate Depot Formulation, (LY170053 Monohydrate Salt)	6. IND NUMBER (if previously assigned) 60,701
7. INDICATION(S) (Covered by this submission) Schizophrenia	
8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED: <input type="checkbox"/> PHASE 1 <input type="checkbox"/> PHASE 2 <input type="checkbox"/> PHASE 3 <input type="checkbox"/> OTHER <u>NA</u> <i>(Specify)</i>	
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SERIAL NUMBER
0 1 6 0

11. THIS SUBMISSION CONTAINS THE FOLLOWING: (Check all that apply)

INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND) RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):	INFORMATION AMENDMENT(S):	IND SAFETY REPORT(S):
<input type="checkbox"/> NEW PROTOCOL	<input type="checkbox"/> CHEMISTRY/MICROBIOLOGY	<input type="checkbox"/> INITIAL WRITTEN REPORT
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<input type="checkbox"/> RESPONSE TO FDA REQUEST FOR INFORMATION	<input type="checkbox"/> ANNUAL REPORT	<input checked="" type="checkbox"/> GENERAL CORRESPONDENCE
<input type="checkbox"/> REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED	<input type="checkbox"/> OTHER <u>Trademark Review</u>	<i>(Specify)</i>

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

TREATMENT IND 21 CFR 312.35(b) TREATMENT PROTOCOL 21 CFR 312.35(a) CHARGE REQUEST/NOTIFICATION 21 CFR 312.7(d)

FOR FDA USE ONLY

CDR/DBIND/DGD RECEIPT STAMP RECEIVED JUN 27 2007 CDER CDR	DDR RECEIPT STAMP RECEIVED JUN 28 2007 CDER White Oak DR 1	DIVISION ASSIGNMENT: IND NUMBER ASSIGNED:
---------------------------------------------------------------------------	----------------------------------------------------------------------------	--------------------------------------------------

12.

CONTENTS OF APPLICATION

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1. Form FDA 1571 [21 CFR 312.23(a)(1)]
2. Table of Contents [21 CFR 312.23(a)(2)]
3. Introductory statement [21 CFR 312.23(a)(3)]
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6. Protocol(s) [21 CFR 312.23(a)(6)]
- a. Study protocol(s) [21 CFR 312.23(a)(6)]
- b. Investigator data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
- c. Facilities data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
- d. Institutional Review Board data [21 CFR 312.23(a)(6)(iii)(b)] or completed Form(s) FDA 1572
7. Chemistry, manufacturing, and control data [21 CFR 312.23(a)(7)]
- Environmental assessment or claim for exclusion [21 CFR 312.23(a)(7)(iv)(e)]
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13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? YES NOIF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? YES NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

Dr. Sara Corya
Medical Director-Zyprexa

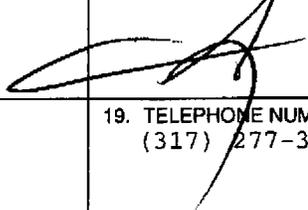
15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set forth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE

Gregory T. Brophy, Ph.D.
Director
US Regulatory Affairs

17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE



18. ADDRESS (Number, Street, City, State and Zip Code)

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

19. TELEPHONE NUMBER (Include Area Code)

(317) 277-3799

20. DATE

6/26/07

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Amundson Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please DO NOT RETURN this application to this address.

IND 60,701

LY170053

Sponsor's Serial No. 0160

IND Table Of Contents

Module Section Number	Description	Volume Number
	Cover Letter	
	FDA Form 1571	1
	Table of Contents	1
	Request for Trademark Review	
	Appendix 1: FDA letter Dated May 24, 2007	1
	Literature References	
	Appendix 2: Literature References	1

Appendix 1: FDA Letter Dated May 24, 2007

Appendix 2: Literature References (Available Upon Request)

Cited References:

Adams CE, Fenton MK, Quraishi S, David AS. Systematic meta-review of depot anti-psychotic drugs for people with schizophrenia. *British Journal of Psychiatry*. 2001;179:290-299.

Babiker IE, Comparative efficacy of long-acting depot and oral neuroleptic medications in preventing schizophrenic recidivism, *Journal of Clinical Psychiatry* 1987;48: 94-97.

Barnes TR, Curson DA. Long-term depot anti-psychotics. A risk-benefit assessment. *Drug Safety*. 1994;10:464-479

Davis JM, Metalon L, Watanabe MD, Blake L. Depot antipsychotic drugs. Place in therapy. *Drugs* 1994;47(5):741-773.

Diaz E, Levine HB et al. Use of the Medication Event Monitoring System to estimate medication compliance in patients with schizophrenia. *Journal of Psychiatry & Neuroscience* 2001;26(4):325-329.

Haro JM, Edgell ET, Frewer P, Alonso J, Jones PB, SOHO Study Group. The European Schizophrenia Outpatient Health Outcomes Study: baseline findings across country and treatment. *Acta Psychiatrica Scandinavica, Supplementum*. 2003;7-15.

Remington GJ, Adams ME. Depot neuroleptic therapy: clinical considerations. *Canadian Journal of Psychiatry*. 1995;40 Suppl. 1:S5-S11.

Additional References:

Kane JM. Strategies for improving compliance in treatment of schizophrenia by using a long-acting formulation of an antipsychotic: clinical studies. *Journal of Clinical Psychiatry*. 2003;64 Suppl 16:34-40.

McEvoy JP. Risks versus benefits of different types of long-acting injectable antipsychotics. *Journal of Clinical Psychiatry* 2006;67(Suppl 5):15-18.

Schooler NR. Relapse and rehospitalization: comparing oral and depot antipsychotics. *Journal of Clinical Psychiatry* 2003;64(Suppl 16):14-17.

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/s/

Thomas Laughren
7/18/2007 04:28:21 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD- 420 Division of Medication Errors and Technical Support (DMETS) Attention: Angela Robinson		FROM: HFD-130 / Division of Psychiatry Products Keith Kiedrow, Regulatory Project Manager		
DATE July 18, 2007	IND NO. 60,701 N160	NDA NO. 22-173 leter date June 26, 2007	TYPE OF DOCUMENT tradename review request – rebuttal by sponsor to issued letter	DATE OF DOCUMENT June 26, 2007
NAME OF DRUG Zyprexa Adhera (olanzapine long acting injection)		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG Schizophrenia	DESIRED COMPLETION DATE August 31, 2007
NAME OF FIRM: Lilly				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Attached is a rebuttal from Lilly to the letter we (DPP) issued to the sponsor regarding their initial tradename, Adhera, for Zyprexa Long Acting Injection. I've also attached the letter that was issued. Please review and provide comments regarding the validity of their arguments. Thanks!				
SIGNATURE OF REQUESTER LCDR Keith Kiedrow, Pharm.D. Regulatory Project Manager 301-796-1924 keith.kiedrow@fda.hhs.gov		METHOD OF DELIVERY (Check one) x MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

12 pages of
Admin_LillyConfidential has been
withheld in full immediately following
this page as B4 CCI/TS

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Thomas Laughren
7/18/2007 04:28:21 PM

DSI CONSULT: Request for Clinical Inspections

Date: July 2, 2007

To: Leslie Ball, M.D., Branch Chief, GCP2, HFD-47

cc: Joseph Salewski, , Acting Director, DSI, HFD-45
Thomas Laughren, M.D., Director, HFD-130

From: Keith Kiedrow, Regulatory Project Manager, HFD-130
Division of Psychiatry Products

Subject: Request for Clinical Site Inspections
NDA 22-173
Eli Lilly and Company
Zyprexa (olanzapine) long acting injection
Sponsor contact information –

Matt Kuntz, R.Ph., M.B.A.
U.S. Regulatory Affairs
Eli Lilly and Company
Ph 317.433.1766
KUNTZ_MATT@LILLY.COM

Protocol/Site Identification:

As discussed with you, the following protocols/sites essential for approval have been identified for inspection. These sites are listed in order of priority. Sites were chosen due to high number of enrollees.

Study F1D-MC-HGJZ

Site #	Principal Investigator	Site & Address	# pts Randomized
16	Brams, Matthew	Bayou City Research Corp. 550 Westcott, Suite 310 Houston, Texas 77007	28
31	Litman, Robert Enoch	CBH Health, LLC 9605 Medical Center Drive Main Office: Suite 250 Rockville, MD 20850	25
32	Lowry, Adam F.	Psychiatric Institute of Washington	15

		DC 4228 Wisconsin Avenue, NW Washington, DC 20016	
--	--	---------------------------------------------------------	--

Domestic Inspections:

We have requested inspections because (please check all that apply):

- Enrollment of large numbers of study subjects
- High treatment responders (specify:)
- Significant primary efficacy results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
- Other: SPECIFY

International Inspections:

We have requested inspections because (please check all that apply):

- There are insufficient domestic data
- Only foreign data are submitted to support an application
- Domestic and foreign data show conflicting results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, or significant human subject protection violations.
- Other: SPECIFY

Goal Date for Completion:

We request that the inspections be performed and the Inspection Summary Results be provided by December 14, 2007. The PDUFA due date for this application is February 29, 2008.

Should you require any additional information, please contact Keith Kiedrow,
Keith.Kiedrow@fda.hhs.gov.

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/s/

Thomas Laughren
7/5/2007 12:15:09 PM

REQUEST FOR CONSULTATION

TO (Office/Division): Sylvia Gantt for David Hussong and James McVey, NEW DRUG MICROBIOLOGY STAFF OC/OO/CDER/OPS/NDMS - HFD-805

FROM (Name, Office/Division, and Phone Number of Requestor): Scott N. Goldie, PhD for David Claffey, PhD Division of Pre-Marketing Assessment I, Off. of New Drug Quality Assessment

DATE
June 28, 2007

IND NO.

NDA NO.
22-173

TYPE OF DOCUMENT
Original NDA

DATE OF DOCUMENT
April 27, 2007

NAME OF DRUG
Zyprexa/Adhera (olanzapine long-acting injection)

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
November 12, 2007

NAME OF FIRM: Eli Lilly and Company

REASON FOR REQUEST

I. GENERAL

- | | | |
|----------------------------------------------------------|--------------------------------------------------|-----------------------------------------------------------------|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input checked="" type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|-------------------------------------------------|-------------------------------------------------|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--------------------------------------------------|------------------------------------------------------|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
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| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
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COMMENTS / SPECIAL INSTRUCTIONS: Microbiology review requested of New NDA application. Please direct questions to David Claffey, PhD at 61343 or Prafull Shiromani at 62133. Electronic Submission in EDR:
\\cdesub1\nonectd\n22173\N_00\2007-04-30.

SIGNATURE OF REQUESTOR
{See appended electronic signature page}

METHOD OF DELIVERY (Check one)
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/s/

Ramesh Sood
6/29/2007 10:56:02 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD- 715 /Biometrics Attention: Karl Lin		FROM: HFD-130/Div. of Psychiatry Products		
DATE May 21, 2007	IND NO.	NDA NO. 22-173	TYPE OF DOCUMENT New NDA submission	DATE OF DOCUMENT April 27, 2007
NAME OF DRUG Zyprexa (olanzapine) Adhera long acting injection		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE December 1, 2007
NAME OF FIRM: Lilly				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Dr. Lin, Lilly submitted, on April 27, 2007, a new NDA for a long acting injectable form of Zyprexa. Per the pharm/tox reviewer, Sonia Tabacova, the submission contains preclinical carcinogenicity studies. Please review and comment on the carcinogenicity studies. The primary PDUFA goal date for this NDA is 2/29/2008. Our filing goal date is 6/29/2007 and the filing meeting is scheduled for 6/19/2007. This application has been submitted electronically and may be accessed by the electronic document room (EDR) @ \\CDSESUB1\NONECTD\N22173\N_000\2007-04-30. Please provide, via email, an attendee (or attendees) that will be available for the filing meeting. Should you have any questions, please contact me at via the contact information below.				
SIGNATURE OF REQUESTER Keith Kiedrow, Pharm.D. Regulatory Project Manager 301-796-1924 keith.kiedrow@fda.hhs.gov		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Thomas Laughren
5/22/2007 03:25:44 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD- 710 /Biometrics Attention: Peiling Yang, PhD		FROM: HFD-130 (Division of Psychiatry Products); Keith Kiedrow		
DATE May 9, 2007	IND NO.	NDA NO. 22-173	TYPE OF DOCUMENT New NDA	DATE OF DOCUMENT April 27, 2007
NAME OF DRUG Zyprexa Adhera		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE Reviews due to clin TL 1/28/2008
NAME OF FIRM: Lilly				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: The following is a link to a new NDA for Zyprexa Adhera (olanzapine long acting injection) - \\CDSESUB1\NONECTD\N22173\N_000\2007-04-30. It is indicated for the treatment of schizophrenia. Please review from a statistical perspective. The PDUFA due date for this application is 2/29/08, please have reviews completed and available for review by 1/11/08. Thanks.				
SIGNATURE OF REQUESTER Keith Kiedrow, Pharm.D. Regulatory Project Manager 301-796-1924 keith.kiedrow@fda.gov		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> HAND		
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/s/

Keith Kiedrow

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): HFD- 860/Biopharm / Ray Baweja		FROM: HFD-130 (Division of Psychiatry Products); Keith Kiedrow		
DATE May 9, 2007	IND NO.	NDA NO. 22-173	TYPE OF DOCUMENT New NDA	DATE OF DOCUMENT April 27, 2007
NAME OF DRUG Zyprexa Adhera		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE Reviews due to clin TL 1/28/2008
NAME OF FIRM: Lilly				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: The following is a link to a new NDA for Zyprexa Adhera (olanzapine long acting injection) - \\CDSESUB1\NONECTD\N22173\N_000\2007-04-30. It is indicated for the treatment of schizophrenia. Please review from an OCPB perspective. The PDUFA due date for this application is 2/29/08, please have reviews completed and available for review by 1/11/08. Thanks.				
SIGNATURE OF REQUESTER Keith Kiedrow, Pharm.D. Regulatory Project Manager 301-796-1924 keith.kiedrow@fda.gov		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Keith Kiedrow
5/9/2007 03:20:10 PM

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22-173 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Relprev Established/Proper Name: olanzapine pamoate Dosage Form: For Extended Release 210 mg, 300 mg, and 405 mg Injectable Suspension		Applicant: Eli Lilly and Company Agent for Applicant (if applicable):
RPM: Keith Kiedrow		Division: Division of Psychiatry Products
<p>NDA: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> <p>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</p>
❖ User Fee Goal Date Action Goal Date (if different)		AP December 11, 2009 CR September 12, 2009 NA December 11, 2009
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (<i>specify type and date for each action taken</i>)		CR – December 15, 2008 NA – February 25, 2008

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

<p>❖ Promotional Materials (<i>accelerated approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance www.fda.gov/cder/guidance/2197dft.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application² Characteristics</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 1</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC</p> <p>Comments: _____</p>	
<p>❖ Date reviewed by PeRC (<i>required for approvals only</i>) If PeRC review not necessary, explain: _____</p>	<p>October 29, 2008</p>
<p>❖ BLAs only: <i>RMS-BLA Product Information Sheet for TBP</i> has been completed and forwarded to OBPS/DRM (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes, date
<p>❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Indicate what types (if any) of information dissemination are anticipated 	<input type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input checked="" type="checkbox"/> Other: information advisory

² All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLA: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	N/A
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	N/A
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	N/A
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	N/A
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	N/A
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	N/A

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

N/A

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist ³	Yes
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) AP - September 11, 2009 CR - December 15, 2008 NA - February 25, 2008
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	Identical to label agreed upon with sponsor and included with the AP letter
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	No
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	3/11/09 resubmission label 6/13/08 resubmission label 4/30/07 original submission label
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	No
❖ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>)	<input checked="" type="checkbox"/> Medication Guide (Included with AP letter)

³ Fill in blanks with dates of reviews, letters, etc.
Version: 9/5/08

	<input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
❖ Labels (full color carton and immediate-container labels) (write submission/communication date at upper right of first page of each submission)	
<ul style="list-style-type: none"> • Most-recent division proposal for (only if generated after latest applicant submission) 	N/A
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	No
❖ Labeling reviews (indicate dates of reviews and meetings)	Contained in various discipline reviews and DMEPA/OSE reviews 5/31/07 3/6/08 4/3/08 1/9/09 6/18/09 8/4/09
❖ Proprietary Name <ul style="list-style-type: none"> • Review(s) (indicate date(s)) • Acceptability/non-acceptability letter(s) (indicate date(s)) 	DMEPA reviews listed above in labeling reviews AP Letter 9/11/2009
Administrative / Regulatory Documents	
❖ Administrative Reviews (e.g., RPM Filing Review⁴/Memo of Filing Meeting) (indicate date of each review)	No
❖ NDAs only: Exclusivity Summary (signed by Division Director)	<input checked="" type="checkbox"/> 9/11/09
❖ Application Integrity Policy (AIP) Status and Related Documents www.fda.gov/ora/compliance_ref/aip_page.html	
<ul style="list-style-type: none"> • Applicant in on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (indicate date) ○ If yes, OC clearance for approval (indicate date of clearance communication) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatric Page (approvals only, must be reviewed by PERC before finalized)	<input checked="" type="checkbox"/> reviewed by PERC, in darrts as peds entry
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (include certification)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Requirement (PMR) Studies	N/A

⁴ Filing reviews for other disciplines should be filed behind the discipline tab.

<ul style="list-style-type: none"> Outgoing communications (<i>if located elsewhere in package, state where located</i>) 	N/A
<ul style="list-style-type: none"> Incoming submissions/communications 	See above
❖ Postmarketing Commitment (PMC) Studies	n/a
<ul style="list-style-type: none"> Outgoing Agency request for postmarketing commitments (<i>if located elsewhere in package, state where located</i>) 	
<ul style="list-style-type: none"> Incoming submission documenting commitment 	
❖ Outgoing communications (<i>letters (except previous action letters), emails, faxes, telecons</i>)	
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> PeRC (<i>indicate date; approvals only</i>) 	email of 12/12/08 included (decision changed to waiver later post approval of Zyprexa pediatric applications)
<ul style="list-style-type: none"> Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) 	N/a – ose involvement all through review cycle
<ul style="list-style-type: none"> Regulatory Briefing (<i>indicate date</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> Pre-NDA/BLA meeting (<i>indicate date</i>) 	Meeting minutes included – 11/26/08 5/14/08 8/14/07 7/24/06 3/10/06 10/7/05 4/28/04
<ul style="list-style-type: none"> EOP2 meeting (<i>indicate date</i>) 	See above
<ul style="list-style-type: none"> Other (e.g., EOP2a, CMC pilot programs) 	See above
❖ Advisory Committee Meeting(s)	<input type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> Date(s) of Meeting(s) 	2/6/2008
<ul style="list-style-type: none"> 48-hour alert or minutes, if available 	Not available
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	2/24/08 1/8/08
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	12/11/09 9/10/09 12/9/08 2/12/08
Clinical Information⁵	
❖ Clinical Reviews	
<ul style="list-style-type: none"> Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	Same as CDTL reviews above
<ul style="list-style-type: none"> Clinical review(s) (<i>indicate date for each review</i>) 	7/22/09 12/8/08 2/19/08 1/7/08

⁵ Filing reviews should be filed with the discipline reviews.

<ul style="list-style-type: none"> Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None
❖ Safety update review(s) (<i>indicate location/date if incorporated into another review</i>)	In clinical reviews above
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	In clinical reviews above
❖ Clinical reviews from other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	N/A
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Risk Management <ul style="list-style-type: none"> Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) REMS Memo (<i>indicate date</i>) REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) 	OSE reviews/memos – 10/23/09 9/11/09 7/21/09 12/24/08 12/15/08 12/13/08
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	4/8/08 4/7/08 12/14/07 8/27/07
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	2/15/08
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	12/18/07
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	N/A
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	8/17/09 11/7/08 2/12/08
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	See DSI reviews above
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
<ul style="list-style-type: none"> ADP/T Review(s) (<i>indicate date for each review</i>) 	n/a
<ul style="list-style-type: none"> Supervisory Review(s) (<i>indicate date for each review</i>) 	N/A
<ul style="list-style-type: none"> Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>) 	2/7/08
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	7/27/07
❖ ECAC/CAC report/memo of meeting	12/13/07

❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested
CMC/Quality <input type="checkbox"/> None	
❖ CMC/Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>)	None
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	11/13/08 2/19/08
• CMC/product quality review(s) (<i>indicate date for each review</i>)	7/8/09 11/13/08 10/28/08 2/19/08 6/19/07 1/31/08
• BLAs only: Facility information review(s) (<i>indicate dates</i>)	N/A
❖ Microbiology Reviews	See microbiology review above
• NDAs: Microbiology reviews (sterility & pyrogenicity) (<i>indicate date of each review</i>)	
• BLAs: Sterility assurance, product quality microbiology (<i>indicate date of each review</i>)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	10/23/07
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ NDAs: Methods Validation	<input checked="" type="checkbox"/> Completed (per CMC review) <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
❖ Facilities Review/Inspection	
• NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>)	Date completed: see CMC reviews <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
• BLAs: <ul style="list-style-type: none"> ○ TBP-EER ○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (<i>date completed must be within 60 days prior to AP</i>) 	N/A

Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.