

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-992

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 21-992

SUPPL #

HFD # 130

Trade Name Pristiq

Generic Name desvenlafaxine succinate

Applicant Name Wyeth Pharmaceuticals, Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 20-151

Effexor (Venlafaxine HCl) Tablets

**Desvenlafaxine is the active metabolite of the parent drug venlafaxine

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study 332 & Study 333

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study 332 & Study 333

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1
IND # 64,552 YES ! NO
! Explain:

Investigation #2
IND # 64,552 YES ! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !
!
YES ! NO
Explain: ! Explain:

Investigation #2 !
!
YES ! NO
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

Name of person completing form: Paul David
Title: CPMS
Date: 2-27-09

Name of Office/Division Director signing form: Thomas Laughren, MD
Title: Division Director, DPP

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

**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
2/27/2008 02:18:32 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-992 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: August 29, 2007 PDUFA Goal Date: February 29, 2008

HFD 130 Trade and generic names/dosage form: Pristiq (desvenlafaxine succinate)

Applicant: Wyeth Pharmaceuticals, INC. Therapeutic Class: 2020100

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- Yes. Please proceed to the next question.
 No. PREA does not apply. Skip to signature block.

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): _____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: Major Depressive Disorder

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
 No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
 No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 0 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 6 Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 7 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 17 Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

NDA 21-992

Page 3

This page was completed by:

{See appended electronic signature page}

Renmeet Grewal, Pharm.D.

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

Yes. PREA does not apply. Skip to signature block.

No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Adult studies ready for approval

Formulation needed

Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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

/s/

Renmeet Grewal
2/26/2008 05:35:33 PM

ACTION PACKAGE CHECKLIST

Application Information		
BLA # NDA # 21-992	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type
Proprietary Name: Pristiq Established Name: desvenlafaxine succinate Dosage Form: tablets		Applicant: Wyeth
RPM: Renmeet Grewal, Pharm.D.		Division: DPP Phone # 301-796-1080
NDAs: 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) (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.)		505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): Provide a brief explanation of how this product is different from the listed drug. <input type="checkbox"/> If no listed drug, check here and explain: Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct. <input type="checkbox"/> Confirmed <input type="checkbox"/> Corrected Date:
❖ User Fee Goal Date ❖ Action Goal Date (if different)		February 29, 2008
❖ 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>)		<input type="checkbox"/> None AE (2/22/07)
❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)		<input checked="" type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 1	
NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2 <input type="checkbox"/> Orphan drug designation	
NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies	BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies
NDAs and NDA Supplements: <input type="checkbox"/> OTC drug Other: Other comments:	
❖ Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> Applicant is 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"> Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action 	<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 checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

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)?

Yes No

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 (3).

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

Yes No

(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)?

Yes No

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).

- (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?

Yes No

(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

<p>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 Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</i></p>	
Summary Reviews	
<ul style="list-style-type: none"> ❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review) 	<p>Office Director (2/29/08) Division Director (2/20/08) (1/16/07) Deputy Division Director (11/8/06) CDTL (2/5/08)</p>
<ul style="list-style-type: none"> ❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date) 	
Labeling	
<ul style="list-style-type: none"> ❖ Package Insert 	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	2/29
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<ul style="list-style-type: none"> ❖ Patient Package Insert 	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	N/A
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	N/A
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	N/A
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	N/A
<ul style="list-style-type: none"> ❖ Medication Guide 	
<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 applicant-proposed 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) 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) 	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) 	2/29
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	

❖ Labeling reviews and minutes of any labeling meetings (<i>indicate dates of reviews and meetings</i>)	<input checked="" type="checkbox"/> DMETS <input checked="" type="checkbox"/> DSRCS <input type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input type="checkbox"/> Other reviews <input type="checkbox"/> Memos of Mtgs
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Administrative Documents

❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) (<i>indicate date of each review</i>)	3/1/06
❖ NDA and NDA supplement approvals only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> • Center Director's Exception for Review memo • If AP: OC clearance for approval 	
❖ Pediatric Page (all actions)	X Included
❖ 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. (<i>Include certification.</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies <ul style="list-style-type: none"> • Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>) • Incoming submission documenting commitment 	<input type="checkbox"/> None Located in AP letter
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	X
❖ Internal memoranda, telecons, email, etc.	X
❖ Minutes of Meetings <ul style="list-style-type: none"> • Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) • Pre-NDA/BLA meeting (<i>indicate date</i>) • EOP2 meeting (<i>indicate date</i>) • Other (e.g., EOP2a, CMC pilot programs) 	<input type="checkbox"/> No mtg <input type="checkbox"/> No mtg
❖ Advisory Committee Meeting <ul style="list-style-type: none"> • Date of Meeting • 48-hour alert or minutes, if available 	<input checked="" type="checkbox"/> No AC meeting
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	

CMC/Product Quality Information

❖ CMC/Product review(s) (<i>indicate date for each review</i>)	A/E:
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications) <ul style="list-style-type: none"> • <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>) • <input checked="" type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) • <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) 	4/12/06 4/5/06
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (<i>indicate date of each review</i>)	

	<input type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection	
❖ NDAs: Facilities inspections (include EER printout)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed

Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	2/5/08 & 1/22/07
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input type="checkbox"/> No carc 1/10/07
❖ ECAC/CAC report/memo of meeting	
❖ Nonclinical inspection review Summary (DSI)	<input checked="" type="checkbox"/> None requested

Clinical Information	
❖ Clinical review(s) (<i>indicate date for each review</i>)	11/6/06, 1/29/08
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	<input type="checkbox"/> None 8/3/06
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	Met with OSE regarding the RISKMAP. We sent the sponsor an IR letter
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	1/17/07
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	<input type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested
<ul style="list-style-type: none"> • Clinical Studies • Bioequivalence Studies • Clin Pharm Studies 	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/10/08, 8/3/06,
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 1/28/08, 10/26/06

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 Office of Regulatory Policy representative.

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/s/

Renmeet Grewal

3/4/2008 04:17:44 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992

ADVICE LETTER

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Venkateshwaran:

Please refer to your December 22, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pristiq® (desvenlafaxine succinate) extended release tablets.

We also refer to your correspondence dated February 2, 2007, requesting clarification on what the Reference Listed Drug name will be for your product. We confirm that, if the established name on the DVS product labeling is the base (desvenlafaxine), the Reference Listed Drug name will be desvenlafaxine succinate, not desvenlafaxine. Refer to the Orange Book for multiple examples of this scenario.

If you have any questions, call Amy Bertha, Project Manager, at (301) 796-1647.

Sincerely,

Chi-wan Chen, Ph.D.
Deputy Director
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Michael Folkendt
2/27/2007 03:58:19 PM
Signed for Dr. Chi-wan Chen.



NDA 21-992

INFORMATION REQUEST LETTER

Wyeth-Ayerst Research
Attention: Kenneth Bonk
Associate Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Bonk:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Desvenlafaxine Succinate 50mg, 100mg, and 200mg extended release tablets.

We also refer to your submission dated September 7, 2006 and August 15, 2007 regarding the RiskMap.

The Office of Surveillance and Epidemiology has the following comments and information requests regarding your RiskMap plan for Desvenlafaxine. We request a prompt written response in order to continue our evaluation of your NDA.

Elements in the venlafaxine RiskMAP, including an educational program similar to that proposed for desvenlafaxine, and unit-of-use packaging, were implemented in 2005 and 2006. Information about the impact of the venlafaxine RiskMAP should help inform us about the potential impact of the proposed RiskMAP for desvenlafaxine. We have the following questions regarding desvenlafaxine:

1. Are there any differences between the educational program you have implemented for venlafaxine and the education you propose for the desvenlafaxine RiskMAP? Please provide us details regarding what is the same, and what is different between the education implemented for venlafaxine and what is proposed for desvenlafaxine:
 - a. For prescribers
 - b. For pharmacists
 - c. For patients

Please submit the educational materials in place for the venlafaxine RiskMAP, and the educational materials proposed for the desvenlafaxine RiskMAP.

2. Does the venlafaxine RiskMAP include a provision to measure the impact of the educational program implemented? For example, have you surveyed participants to

measure the results of your educational efforts? Please provide us with the results of any such measurements.

3. Please provide data regarding the unit-of-use packages of venlafaxine.
 - a. How many such packages have been dispensed by physicians (i.e., sampling) (please provide data by quarter, product, and physician specialty)?
 - b. Since implementation of the unit-of-use packages, how many prescriptions have been written and dispensed for unit-of-use packages (please provide data by quarter, product, and physician specialty)?
 - c. What proportion of the venlafaxine market comprise the unit-of-use packages?
 - d. To what extent do pharmacies dispense the unit-of-use packages when prescribed by physicians? What barriers have you discovered to pharmacist use of the unit-of-use packages?
 - e. For what diagnoses have these packages been dispensed?
 - i. To what extent have these packages been prescribed/dispensed during periods of higher suicidal risk?
 - f. Provide your assessment of the success of the unit-of-use packaging in minimizing suicidal risk during periods of higher risk.

4. Have you undertaken assessment of the impact of the risk minimization elements in place for venlafaxine on the incidence of suicide attempts, successful suicides, and/or fatal overdoses for patients receiving venlafaxine? Please provide us with your assessment of the impact of your efforts on these outcomes.

Please provide the agency with a timeframe regarding the response to the questions above.

If you have any questions, call Renmeet Grewal, Pharm.D., Regulatory Project Manager, at 301-796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Thomas Laughren
1/25/2008 04:55:05 PM

Grewal, Renmeet

From: Grewal, Renmeet
Sent: Monday, December 17, 2007 2:55 PM
To: 'Kenneth Bonk'
Subject: NDA 21-992

Hi Ken,

Can you please respond to the request below by the end of this week:

- For both studies 332 and 333, study visits were scheduled at Baseline, Week 1, Week 2, Week 3, Week 4, Week 6 and Week 8 (i.e., Days 1, 7, 14, 21, 28, 42, and 56). However, according to the data files that you provided, we found that some patients had Week 5 and/or Week 7 data in addition to these weeks data. It is not clear why only 6% to 9% of total patients had data for these weeks. Please clarify this point. In addition, please provide us with the data with the dates of visits for each patient in a SAS transport data file.
- Please perform the MMRM analysis by using the unstructured covariance matrix after cleaning your data with only Baseline, Week 1, Week 2, Week 3, Week 4, Week 6 and Week 8 data for each patient.

Thank you,
Rimmy

*Renmeet Grewal, Pharm.D., LCDR USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Ph: (301) 796-1080
Email: renmeet.grewal@fda.hhs.gov
Fax: (301) 796-9838*

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/s/

Renmeet Grewal
12/17/2007 03:00:49 PM
CSO



NDA 21-992
NDA 21-966

INFORMATION REQUEST LETTER

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Venkateshwaran:

Please refer to your new drug applications (NDAs) 21-992, dated December 22, 2005, and 21-966, dated June 23, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for desvenlafaxine extended release tablets.

We are reviewing your amendment dated August 23, 2007 to NDAs 21-992 and 21-966 regarding the proposed Comparability Protocol (CP) for the Implementation of Real Time Release (RTR) of desvenlafaxine extended release tablets, and have the following questions pertaining to the sampling and specification for real time release.

1. With reference to the tablet assay _____ summarize the sampling plan, in a tabular format, that represents the batch in terms of sampling frequency and sample size at each sampling point for each tablet strength, batch size, and tablet _____ for commercial production.

Explain the statistical basis for the selected sample sizes for dose uniformity and _____ assay. Additionally, for each specified sample size, indicate the confidence interval (e.g., _____) at which the quality of the drug product can be ensured.

Clarify the discrepancy between having an _____

2. The proposed criteria for DVS



3. The currently proposed criterion for l _____



We will provide comments at a later date concerning information to be included in your intended supplemental application when implementing real time release according to the CP.

If you have any questions, call Amy Bertha, Regulatory Health Project Manager, at 301-796-1647.

Sincerely,

{See appended electronic signature page}

Chi-wan Chen, Ph.D.
Deputy Director
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Chi Wan Chen

11/9/2007 02:44:31 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992

Wyeth Pharmaceuticals Inc.
Attention: Kenneth R. Bonk
Director II, Global Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101

Dear Mr. Bonk:

We acknowledge your submission dated and received on August 29, 2007 to your new drug application for Desvenlafaxine succinate 50mg, 100mg, 200mg tablets.

We consider this a complete, class 2 response to our January 22, 2007 action letter. Therefore, the user fee goal date is February 29, 2008.

If you have any questions you can call me at (301) 796-1080.

Sincerely,

{See appended electronic signature page}

Renmeet Grewal, Pharm.D.
Senior Regulatory Project Manager
Division of Psychiatry
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Renmeet Grewal

10/16/2007 09:27:34 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992

NDA 21-996

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Venkateshwaran:

Please refer to your new drug applications (NDAs) 21-992, dated December 22, 2005, and 21-966, dated June 23, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for desvenlafaxine extended release tablets.

We refer to the meeting between representatives of your firm and the FDA on May 22, 2007. The purpose of the meeting was to discuss the questions and comments provided in the IR letter dated May 3, 2007.

The official minutes of the above meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me, at (301) 796-1647.

Sincerely,

{See appended electronic signature page}

Amy Bertha
Regulatory Health Project Manager
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Enclosure

MEMORANDUM OF MEETING MINUTES

JUL - 5 2007

MEETING DATE: May 22, 2007
TIME: 2:00 pm- 3:30 pm
LOCATION: Food and Drug Administration, White Oak Room 1417
APPLICATION: NDA 21-992 & NDA _____
DRUG NAME: Desvenlafaxine succinate extended-release tablets
TYPE OF MEETING: Type C
MEETING CHAIR: Chi-wan Chen
MEETING RECORDER: Amy Bertha

FDA ATTENDEES:

OFFICE OF NEW DRUG QUALITY ASSESSMENT

Chi-wan Chen, Deputy Directory
Thomas Oliver, Pharmaceutical Assessment Lead, Division of Pre-Marketing Assessment I
Mike Adams, Review Chemist, Division of Pre-Marketing Assessment III
Terrance Ocheltree, Review Chemist, Manufacturing Sciences Branch
Vibhakar Shah, Chemist, Regulatory Science and Policy Staff
Amy Bertha, Regulatory Health Project Manager

OFFICE OF COMPLIANCE

Zi Qiang Gu, Compliance Officer
Muralidhara Gavini, Compliance Officer

EXTERNAL CONSTITUENT ATTENDEES from Wyeth:

Chunsheng Cai, Principal Quality Scientist, Analytical Development, Global Quality Operations
Lori Henning, Senior Director, Global Quality Operations
Carl Longfellow, Director, Analytical and Quality Sciences
Patricia Foti Mann, Senior Director, Global Regulatory Affairs, CMC
Carlos Conde-Reyes, Director, PAT Development, Global Technology Services
Vicente Rosado, Associate Director, Quality Operations, DVS-233 Primary Processing Unit.
Shailesh Singh, Principal Research Scientist II, Preclinical Development
T.G. Venkateshwaran, Associate Director, Global Regulatory Affairs, CMC
Dominic Ventura, Vice President, Global Technology Services

BACKGROUND:

The NDAs for desvenlafaxine succinate extended-released tablets were accepted into the CMC pilot program on September 1, 2005. NDA 21-992 was submitted on December 22, 2005, and NDA _____ was submitted on _____ the purpose of this meeting was for Wyeth to ask clarification questions on the contents of the IR letter dated May 3, 2007. This IR letter focused on the Comparability Protocol for Process Analytical Technology and Real Time Release.

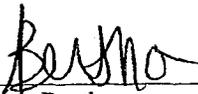
THE MEETING:

Wyeth provided FDA with a briefing package containing slides, which are attached to these minutes. The slides outlined topics that facilitated the discussion of the questions and comments provided in the IR letter. It was agreed by both parties that these minutes would not capture the details of the discussion.

During the discussions, Wyeth said they would address in their response and/or at the POV the statistical basis of the sample plan, that is representative of the batch, to be used for Dose Uniformity by Weigh Variation.

ACTION ITEMS:

Wyeth will send their official response to the IR letter in the form of an NDA amendment.

Minutes Preparer: 
Amy Bertha
Regulatory Health Project Manager
Office of New Drug Quality Assessment

Chair Concurrence: 
Chi-wan Chen
Deputy Director
Office of New Drug Quality Assessment

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/s/

Amy Bertha

7/6/2007 03:53:25 PM

Grewal, Renmeet

From: Grewal, Renmeet
Sent: Wednesday, May 30, 2007 8:26 AM
To: 'Kenneth Bonk'
Cc: Bender, William
Subject: Submission timing for NDA 21-992

Hi Ken,

We have received your submission dated 4/4/07, where you provide an argument, based on your analysis of the totality of the data in rats and rabbits, that the embryo-fetal toxicity study in rats that we requested as a post-marketing commitment would not provide useful information. We will accept this as a complete response to this issue. However, the adequacy of this argument will not be determined until it is reviewed in detail under your formal complete response to our approvable letter.

Sincerely,

Rimmy

*Renmeet Grewal, Pharm.D., LCDR USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Ph: (301) 796-1080
Email: renmeet.grewal@fda.hhs.gov
Fax: (301) 796-9838*

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/s/

Renmeet Grewal
5/30/2007 08:42:36 AM
CSO

MEMORANDUM OF TELECON

DATE: November 30, 2006

APPLICATION NUMBER: NDA 21-992, desvenlafaxine succinate ER Tablets

BETWEEN:

Name: Arwinder Nagi, Senior Director, Pharmaceutical Development
Lori Henning, Senior Director, Global Quality Operations
Carl Longfellow, Director, Analytical and Quality Sciences
Patricia F. Mann, Senior Director, Global Regulatory Affairs – CMC
T.G. Venkateshwaran, Assoc. Director, Global Regulatory Affairs - CMC
Dominic Ventura, Vice President, Global Technology Services
Loren Wrisley, Director, Analytical and Quality Sciences

Representing: Wyeth

AND

Office of New Drug Quality Assessment

Chi-wan Chen, Deputy Director

Tom Oliver, Pharm. Assessment Lead, Division of Pre-Marketing Assessment I

Mike Adams, Chemist, Division of Pre-Marketing Assessment III

Terry Ocheltree, Chemist, Division of Manufacturing Sciences

Amy Bertha, Regulatory Health Project Manager

Representing: FDA

SUBJECT: Clarify questions in November 6, 2006 IR letter

NDA 21-992, desvenlafaxine succinate ER tablets, for major depressive disorder, was submitted on December 22, 2005. A major amendment was submitted on July 31, 2006 extending the PDUFA user fee date to January 22, 2007. This NDA is part of the CMC pilot program. An IR letter was sent on May 5, 2006 and response submitted on July 3, 2006. A second IR letter was issued on November 6, 2006. A teleconference was held on November 14, 2006 at FDA's request to discuss the timelines of the facilities, PAT CP and regulatory agreement. Wyeth requested this teleconference to clarify questions in the November 6, 2006 IR letter. On November 29, 2006 Wyeth sent slides and a literature paper as background for the teleconference which are attached to these minutes.

Meeting Discussion:

- FDA clarified that the objective of this teleconference is to clarify the questions in the November 6, 2006 IR letter and that FDA would not review any responses during the

NDA 21-992
Page 3 of 3

{See appended electronic signature page}

Amy Bertha
Regulatory Health Project Manager

13 Page(s) Withheld

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 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative- 2

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/s/

Amy Bertha
1/25/2007 09:41:31 AM
PROJECT MANAGER FOR QUALITY

MEMORANDUM OF TELECON

DATE: November 14, 2006

APPLICATION NUMBER: NDA 21-992, desvenlafaxine succinate ER Tablets

BETWEEN:

Name: Francis Sakers, Senior Vice President, Global TOPS & Compliance
Dominic Ventura, Vice President, Global Technology Services
Nirdosh Jagota, Assist. Vice President, Global Regulatory Affairs - CMC
Patricia F. Mann, Senior Director, Global Regulatory Affairs - CMC
T.G. Venkateshwaran, Assoc. Director, Global Regulatory Affairs - CMC

Representing: Wyeth

AND

Office of New Drug Quality Assessment

Chi-wan Chen, Deputy Director

Tom Oliver, Pharm. Assessment Lead, Division of Pre-Marketing Assessment I

Mike Adams, Chemist, Division of Pre-Marketing Assessment III

Terry Ocheltree, Chemist, Division of Manufacturing Sciences

Amy Bertha, Regulatory Health Project Manager

Representing: FDA

SUBJECT: Discuss CMC general CMC issues concerning the NDA review.

NDA 21-992, desvenlafaxine succinate ER tablets, for major depressive disorder, was submitted on December 22, 2005. A major amendment was submitted on July 31, 2006 extending the PDUFA user fee date to January 22, 2007. This NDA is part of the CMC pilot program. An IR letter was sent on May 5, 2006 and response submitted on July 3, 2006. A second IR letter was issued on November 6, 2006. FDA requested this teleconference in order to address general high level CMC issues concerning the NDA review.

Meeting Discussion:

- Facilities timelines and expectations: FDA asked Wyeth to provide an update on the resolution of the warning letter that was issued in June 2006 to Wyeth's manufacturing facility in Puerto Rico and its impact on NDA 21-992. Wyeth explained that they have been in contact with the Office of Regulatory Affairs San Juan District, and they will be ready in the latter half of the first quarter 2007 to meet all the commitments outlined in the warning letter letter. FDA mentioned that the action date for NDA 21-992 is January 22, 2006.

- PAT CP timelines/expectations: Wyeth explained that they would be ready in January for PAT implementation

FDA asked if Wyeth expected to launch the product with PAT once the product is approved.

FDA will work with the investigator to schedule a pre-operational visit (POV), and asked when Wyeth would be ready for a POV. Wyeth will be ready at the end of January for a POV. Wyeth further explained that they provided the San Juan district office a document outlining their timelines inspection readiness.

- Regulatory Agreement: FDA informed Wyeth that the CMC regulatory agreement could not be approved at this time, since there is no regulatory pathway allowing for its approval. However, FDA is interested in pursuing the concept of a regulatory agreement and explained that dialogue on the regulatory agreement can continue.
- FDA asked when Wyeth planned on responding to the November 6, 2006 IR letter. Wyeth plans on submitting a response the week of December 4, 2006. FDA explained that the adequacy of the PAT- CP will be based on the outcome of the POV.

{See appended electronic signature page}

Amy Bertha
Regulatory Health Project Manager

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/s/

Amy Bertha
1/23/2007 03:24:42 PM
PROJECT MANAGER FOR QUALITY

MEMORANDUM OF TELECON

DATE: January 11, 2007

APPLICATION NUMBER: NDA 21-992, desvenlafaxine succinate ER Tablets

BETWEEN:

Name: Ferdinando Aspesi, Sn Vice President, Global Conformance & Regulatory
Ken Bonk, Director II, Global Regulatory Affairs
Sindy Candelario-Gonzal, Director, Product Processing Unit, Guayama, PR
Parimal Desai, Vice President, Analytical and Quality Services
Joe Devito, Vice President, Women's Health Care & Product Intro
Lori Henning, Sn Director, Global Quality Operations
Len Figorski, Ass. Director, Package Engineering
Carl Longfellow, Director, Analytical and Quality Sciences
Patricia F. Mann, Senior Director, Global Regulatory Affairs – CMC
Shailesh Singh, Principle Research Scientist II, Preclinical Development
Dominic Ventura, Vice President, Global Technology Services
Loren Wrisley, Director, Analytical and Quality Sciences

Representing: Wyeth

AND

Office of New Drug Quality Assessment

Chi-wan Chen, Deputy Director

Tom Oliver, Pharm. Assessment Lead, Division of Pre-Marketing Assessment I

Mike Adams, Chemist, Division of Pre-Marketing Assessment III

Terry Ocheltree, Chemist, Division of Manufacturing Sciences

Amy Bertha, Regulatory Health Project Manager

Representing: FDA

SUBJECT: Status of CMC review

NDA 21-992, desvenlafaxine succinate ER tablets, for major depressive disorder, was submitted on December 22, 2005. A major amendment was submitted on July 31, 2006 extending the PDUFA user fee date to January 22, 2007. This NDA is part of the CMC pilot program. An IR letter was sent on May 5, 2006 and response submitted on July 3, 2006. A second IR letter was issued on November 6, 2006. A teleconferences were held on November 14, 2006 and November 30, 2006 to discuss the November 6, 2006 IR letter. FDA requested this teleconference to provide Wyeth with a status of the review, especially concerning issues identified in the November 6, 2006 IR letter and Wyeth's response submitted December 8, 2006.

Meeting Discussion:

- FDA requested this meeting to update Wyeth on the status of the CMC review in relation to the PDUFA goal date of January 22, 2006. FDA is committed to facilitate the PAT implementation. The assessment of question 1-5 of the November 6, 2006 IR letter has been completed, however given the complex and extensive nature of the PAT CP the assessment of question 6 has not been completed. In addition to completing the assessment of Wyeth's response to question 6, FDA sees the pre-operational visit (POV) as an integral part of the eventual approval of the CP. Concerning the timing of the POV, FDA commented that it will not take place until the GMP issues at the Guayama, PR site have been resolved. In reference to questions 1-5, FDA does not expect a response from Wyeth until Wyeth has received FDA's comments in writing.
- In reference to question 1 FDA asked Wyeth to include an _____
- In reference to question 2 FDA asked Wyeth to include a particle size specification for _____
- In reference to question 3a) Wyeth's December 8, 2006 response is acceptable. In reference to question 3b) if Wyeth uses 5 factors and 5 sample points, then the F2 calculations will be acceptable.
- In reference to question 4 Wyeth's December 8, 2006 is acceptable.
- In reference to question 5 Wyeth did not choose one of FDA's two options. In the written comments FDA will provide again the format that is needed for the label concerning the established name and strength.
- In reference to question 6 FDA explained that the PAT CP is still under review, and FDA will not convey a partial assessment at the teleconference.
- FDA asked what was Wyeth's plan concerning the timing of the POV and PAT implementation. _____ FDA clarified their official decision is that the POV will not take place until GMP issues have been resolved, and the POV and GMP inspection will not take place at the same time. Wyeth asked if dialogue between the FDA and Wyeth would continue after the action date concerning the PAT CP. FDA reiterated that they are committed to facilitating the PAT implementation and continuing communication.

{See appended electronic signature page}

Amy Bertha
Regulatory Health Project Manager

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/s/

Amy Bertha
1/23/2007 03:58:14 PM
PROJECT MANAGER FOR QUALITY

MEMORANDUM

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

CLINICAL INSPECTION SUMMARY

DATE: December 27, 2006

TO: Renmeet Grewal, Pharm.D., Regulatory Project Manager
Robert Levin, M.D., Clinical Reviewer
Division of Psychiatry Products

THROUGH: Constance Lewin, M.D., M.P.H.
Branch Chief
Good Clinical Practice Branch I
Division of Scientific Investigations

FROM: Andrea Slavin, RN
Consumer Safety Officer
Good Clinical Practice Branch I
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA: 21-992

APPLICANT: Wyeth Pharmaceuticals, Inc.

DRUG: desvenlafaxine succinate

THERAPEUTIC CLASSIFICATION: 1, S

INDICATION: Treatment of major depressive disorder

CONSULTATION REQUEST DATE: January 4, 2006

DIVISION ACTION GOAL DATE: January 22, 2007 (original date was 8/31/06 prior to change in PDUFA date from 10/22/06 to 1/22/07)

PDUFA DATE: January 22, 2007

I. BACKGROUND:

Desvenlafaxine succinate is a new molecular entity classified as a serotonin and norepinephrine reuptake inhibitor (SNRI). It offers the possibility of a new SNRI with improved safety, tolerability, and dosing.

The goals of the inspections were to assess adherence to FDA regulatory requirements; specifically, investigator oversight, protocol compliance, verification of primary efficacy endpoint data, and protection of subjects' rights, safety, and welfare. The sites were selected based on subject enrollment and inspectional history.

The inspections audited the clinical study: #3151A1-306-US, "A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Three Fixed Doses (100 mg, 200 mg, or 400 mg) of DVS-233 SR in Adult Outpatients with Major Depressive Disorder"

In addition, to ensure compliance with FDA regulations for sponsors of clinical investigations, a sponsor inspection was also performed.

Summary Report of Inspections

II. RESULTS (by protocol/site):

Name of CI and site #, if known	City, State	Protocol	Insp. Date	EIR Received Date	Final Classification
Angelo Sambunaris, MD/022	Marietta, GA	306-US	9/18/06 - 11/16/06	pending	pending
Caroline DuPont, MD/005	Rockville, MD	306-US	6/5/06 - 6/13/06	7/12/06	NAI
Michael Greenbaum, MD/009	Libertyville, IL	306-US	6/13/06 - 6/23/06	8/1/06	NAI
Nicholas DeMartinis, MD/004	Farmington, CT	306-US	6/9/06 - 6/20/06	6/27/06	VAI

Sponsor Inspection

Wyeth Pharmaceuticals, Inc.	Collegeville, PA	306-US	6/27/06 - 7/6/06	8/3/2006	NAI
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Key to Classifications

NAI = No deviation from regulations. Data acceptable.

VAI-No Response Requested= Deviations(s) from regulations. Data acceptable.

VAI-Response Requested = Deviation(s) from regulations. See specific comments below for data acceptability

OAI = Significant deviations from regulations. Data unreliable.

1. Angelo Sambunaris, M.D. (site 022, 20 subjects)
 Atlanta Institute of Medicine and Research
 Mariett Clinic
 531 Roselane Street, Suite 430
 Marietta, GA 30060

Observations noted below are based on the Form FDA 483 and communications from the field investigator. The EIR has not yet been received.

- a. What was inspected: At this site, 23 subjects were screened and 20 subjects were randomized. All subjects' records were audited for informed consent, Mini International Neuropsychiatric Interview (MINI), eligibility, adverse events, and primary efficacy endpoint.
- b. Limitations of inspection: None
- c. Significant observations: For 3 subjects (1266, 1267, and 1268), the MINIs originally completed for these subjects were removed and data on the original MINIs were transcribed to another version. The original MINIs were not retained. For 8 subjects (1270, 1273, 1277, 1278, 1279, 1281, 1282, 1283), the date of completion of the MINI is unclear. The date of Dr. Sambunaris' signature (bottom of the MINI) precedes the date of the MINI interview (date in the header). For all subjects' MINIs, Dr. Sambunaris is identified as the completer in the header of the MINI form; however, Dr. Sambunaris states some of the MINIs were completed by study coordinators. This conflicts with the CRFs, which list Dr. Sambunaris as the completer of the MINI.

The MINI completed for subject 1278 is dated as performed on 4/26/04. Dr. Sambunaris' signature is dated 4/8/04. According to the site's scheduling book, this subject was seen on 1/8/04, not 4/8/04.

There is a significant issue at this site regarding the completion of the Hamilton Psychiatric Rating Scale for Depression (HAM-D₁₇) and the Montgomery and Asberg Depression Scale (MADRS). Dr. Sambunaris was using the Wyeth study to train new personnel at his site. For these 2 scales, the trainee would observe while Dr. Sambunaris interviewed the subject; the trainee would then complete the scales based on his/her interpretation of Dr. Sambunaris' interview of the subject. Dr. Sambunaris would review the scales and initial them if he was in agreement with the trainee's assessment. If he did not agree with an assessment he would change it. The trainees were not approved by Wyeth to be raters for this study.

For subjects 1266 and 1268, self-rating scales (WHO-5 Item Well Being Index and Visual Analog Scale-Pain Intensity) do not support that they were completed by the subjects because the "Completer's Initials" are the initials of the study coordinator.

The Atlanta District Office has informed DSI that the field will be recommending an Official Action Indicated (OAI) classification.

- d. When we have completed our review of the EIR and supporting exhibits, we will make a recommendation regarding the acceptability of the data at this site.
2. Caroline DuPont, M.D. (site 005, 21 subjects)
DuPont Clinical Research, Inc.
6191 Executive Boulevard
Rockville, MD 20852
 - a. What was inspected: At this site, 31 subjects were screened; 21 subjects were randomized and 16 subjects completed the study. All 21 randomized subjects' records were audited.
 - b. Limitations of inspection: None
 - c. Significant observations: Two subjects (250 and 254) did not have protocol-required assessments (Sheehan Disability Scale, WHO-5 Well Being Index, and Visual Analog Scale for Pain Intensity) performed at the baseline visit. In addition, subject 255 did not have a PK sample drawn at Day 56.
 - d. Data from this site are acceptable.
 3. Michael Greenbaum, M.D. (site 009, 20 subjects)
Ingenium Clinical Research
1117 S. Milwaukee Avenue, Suite B-6
Libertyville, IL 60048
 - a. What was inspected: At this site, 24 subjects were screened; 20 subjects were randomized and 16 subjects completed the study. All subjects' records were audited for consent forms, primary efficacy endpoint data, and adverse events.
 - b. Limitations of inspection: Because Dr. Greenbaum had been recently inspected (April 2006) and no significant deviations from FDA regulations were observed, an abbreviated inspection was performed focusing on primary efficacy endpoint and adverse event data.
 - c. Significant observations: Per protocol, subject 497 should have been discontinued from the study at the end-of-week 1 visit when the orthostatic BP fell below 90 mm Hg (standing BPs 86/68 and 85/65). In addition, subject 490 did not have a protocol-required lipid panel drawn at Day 56.
 - d. Data from this site are acceptable.

4. Nicholas DeMartinis, M.D. (site 004, 20 subjects)
University of Connecticut Health Center
10 Talcott Notch Road, 3rd Floor East Lobby
Farmington, CT 06030

- a. What was inspected: At this site, 26 subjects were screened; 20 subjects were randomized, and 14 subjects completed the study. All subjects' records were audited.
- b. Limitations of inspection: None
- c. Significant observations: Subjects 186, 187, and 188 should have been excluded from the study for scoring greater than 3 on a single item (verbal report) on the Covi Anxiety Scale at the screening or baseline visit.
- d. Data from this site are acceptable. However, the review division may want to consider the effect, if any, of data for subjects 186, 187, and 188 who were inappropriately enrolled in the study, and may want to consider removing these subjects from data analyses if appropriate.

4. Wyeth Pharmaceuticals, Inc.
500 Arcola Road
Collegeville, PA 19426

- a. What was inspected: Quality assurance and clinical operations, monitoring reports, IRB correspondence, CRFs, data collection, and drug accountability. Forty-four subjects' records were audited.
- b. Limitations of inspection: None
- c. Significant observations: Inspection did not reveal any regulatory violations.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

As stated above, data from Dr. DuPont, Dr. Greenbaum, and Dr. DeMartinis are acceptable.

At this time, we are unable to make a determination regarding the acceptability of the data at Dr. Sambunaris' site. As noted above, there are concerns regarding the process used to complete the HAM-D₁₇ and the MADRS, as well as other discrepancies in subjects' records. The Atlanta District Office has informed DSI that the field will be recommending an Official Action Indicated (OAI) classification. When we have completed our review of the EIR and supporting exhibits, we will make a recommendation regarding the acceptability of the data at this site.

{See appended electronic signature page}

Andrea Slavin, RN
Consumer Safety Officer

CONCURRENCE:

{See appended electronic signature page}

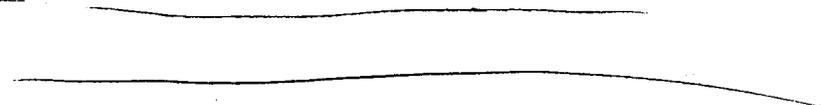
Constance Lewin, M.D., M.P.H.
Branch Chief
Good Clinical Practice Branch I
Division of Scientific Investigations

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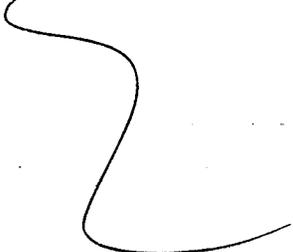
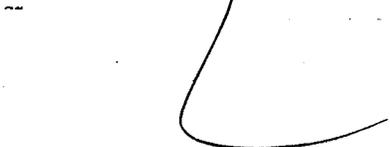
/s/

Andrea Slavin
12/28/2006 10:17:54 AM
CSO

Constance Lewin
12/28/2006 11:23:41 AM
MEDICAL OFFICER

- b. Describe the procedure for comparing the material to the standard and for establishing the 
- c. 
- d. 
- e. Establish a criterion for 
- f. Specify whether the decision to release a product batch 

5. In reference to the method validation study proposed in Protocol P-06-448 we have the following comments:

- a. 
- b. 
- c. 

6. Describe how variability in the  excipients is to be accounted for in the relevant 

If you have any questions, call Amy Bertha, Regulatory Health Project Manager, at 301-796-1647.

Sincerely,

Chi-wan Chen, Ph.D.
Deputy Director
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Chi Wan Chen
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NDA 21-992

INFORMATION REQUEST LETTER

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Venkateshwaran:

Please refer to your December 22, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for desvenlafaxine succinate tablets. Also refer to your amendments dated April 28, July 3, and October 12, 2006.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- 1)  
- 2) Provide further justification for the proposed design space  

- 3) With respect to the Comparability Protocol for the Optimization of Desvenlafaxine Succinate Extended Release Tablet Composition (100 mg formulation):
 - a) 
 - b) 
- 4) Specify whether the proposed blister packages are intended to be child resistant and/or geriatric friendly.
- 5) For the proposed labeling, it is FDA policy that the established name and labeled strength be in agreement with each other.

- 6) The Comparability Protocol for Implementation of PAT and the Implementation of Real Time Release of Desvenlafaxine Succinate Extended Release Tablets is inadequate as currently presented.

- a) The selection criteria for _____


- b) The proposal to _____ does not sufficiently justify the adequacy (i.e., quality and quantity) of the supporting data for PAT implementation. Revise the description of the justification criteria to account for _____
_____ permitted under the proposed design space.

- c) Establish system suitability criteria for each PAT system to ensure that reliable data are collected from the material of interest.
_____ The criteria should be based on variations permitted under the proposed design space.

- d) In reference to the proposed acceptance criteria _____
 - (i)
 - (ii)
 - (iii)
 - (iv)

- f) Regarding the Risk Assessment provisions in Table 1.5-2:
 - (i) Establish a procedure for obtaining a representative sample from a batch in the event of a PAT equipment failure. The procedure should note that any failure of PAT equipment used for real time release (i.e., _____) would require that: A) the affected portion of the batch be isolated; B) a representative sample be taken by a procedure pre-defined in this protocol; and C) the disposition of the batch be determined based on testing per the specification described in NDA section P.5.1.
 - (ii) Include in the Risk Assessment those raw material attributes that should be controlled based on _____
 - (iii) Describe how each PAT measurement will be affected by changes _____

- g) In document GTR-06-139, Evaluation of DVS-233, 100 mg Using PAT, the comparison data showed a _____
Provide an explanation for the _____

If you have any questions, call Amy Bertha, Regulatory Health Project Manager, at 301-796-1647.

Sincerely,

Chi-wan Chen, Ph.D.
Deputy Director
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Chi Wan Chen

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992

Wyeth Pharmaceuticals, Inc.
Attention: Kenneth R. Bonk
Director II
P.O. Box 8299
Philadelphia, PA 19101

Dear Mr. Bonk:

Please refer to your December 22, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (Desvenlafaxine succinate) 100mg, 200mg extended release tablets.

On August 1, 2006, we received your major amendment dated July 31, 2006, to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is January 22, 2007.

If you have any questions, call Renmeet Gujral, Pharm.D. at 301-796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Thomas Laughren
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Venkateshwaran:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for desvenlafaxine succinate extended-release tablet.

We refer to the meeting between representatives of your firm and the FDA on May 23, 2006. The purpose of the meeting was to discuss the questions and comments provided in the IR letter dated May 5, 2006.

The official minutes of the above meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me, at (301) 796-1647.

Sincerely,

{See appended electronic signature page}

Amy Bertha
Regulatory Health Project Manager
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Enclosure

MEMORANDUM OF MEETING MINUTES

JUL 14 2006

MEETING DATE: May 23, 2006
TIME: 2:00 pm- 3:30 pm
LOCATION: Food and Drug Administration, White Oak Room 1415
APPLICATION: NDA 21-992
DRUG NAME: Desvenlafaxine succinate extended-release tablets
TYPE OF MEETING: Type C
MEETING CHAIR: Chi-wan Chen
MEETING RECORDER: Amy Bertha

FDA ATTENDEES:

OFFICE OF NEW DRUG QUALITY ASSESSMENT

Chi-wan Chen, Deputy Directory
Ramesh Sood, Branch Chief, Division of Pre-Marketing Assessment I
Thomas Oliver, Pharmaceutical Assessment Lead, Division of Pre-Marketing Assessment I
Mike Adams, Review Chemist, Division of Pre-Marketing Assessment III
Terrance Ocheltree, Review Chemist, Manufacturing Sciences Branch
Amy Bertha, Regulatory Health Project Manager

OFFICE OF COMPLIANCE

Nick Buhay, Acting Director
Albinus D'Sa, Compliance Officer

EXTERNAL CONSTITUENT ATTENDEES:

Arwinder Nagi, Senior Director, Solids, Pharmaceutical Development,
Richard Saunders, Vice President, Pharmaceutical Development,
Loren Wrisley, Director, Analytical and Quality Sciences, Preclinical Development,
Parimal Desai, Vice President, Analytical and Quality Sciences, Preclinical Development,
Dominic Ventura, Vice President, Global Technology Services,
Nirdosh Jagota, Assistant Vice President, Global Regulatory Affairs- CMC
Patricia F. Mann, Senior Director, Global Regulatory Affairs- CMC
T.G. Venkateshwaran, Senior Manage, Global Regulatory Affairs- CMC

BACKGROUND:

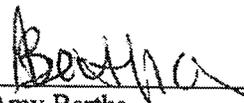
The NDA for desvenlafaxine succinate extended-released tablets was accepted into the CMC pilot program on September 1, 2005, and was submitted to the FDA on December 22, 2005. The purpose of this meeting was for Wyeth to ask clarification questions on the questions and comments provided in the IR letter dated May 5, 2006.

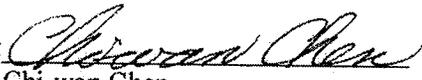
THE MEETING:

Wyeth provided FDA with a briefing package at the meeting which contained (1) a copy of the May 5, 2006 IR letter, (2) a copy of a slide presentation, (3) Wyeth's preliminary responses to the May 5, 2006 IR letter, (4) a copy of the PAT comparability protocol submitted as a supplement to the NDA, (5) Wyeth's proposed Regulatory Agreement submitted in the NDA, and (6) a copy of Section P.3.3 and P.3.4 of the NDA. The slides and preliminary responses, which are attached to these minutes, facilitated the discussion of the questions and comments provided in the IR letter. It was agreed by both parties that these minutes would not capture the details of the discussion. No further requests or recommendations were made outside of what was stated in the May 5, 2006 IR letter.

ACTION ITEMS:

Wyeth will send their official response to the IR letter in the form of an NDA amendment.

Minutes Preparer: 
Amy Bertha
Regulatory Health Project Manager
Office of New Drug Quality Assessment

Chair Concurrence: 
Chi-wan Chen
Deputy Director
Office of New Drug Quality Assessment

22 Page(s) Withheld

X Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-1

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/s/

Amy Bertha

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992

INFORMATION REQUEST LETTER

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran
P.O. Box 8299
Philadelphia, PA 19101-8299

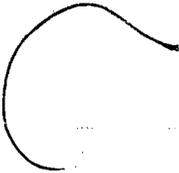
Dear Mr. Venkateshwaran:

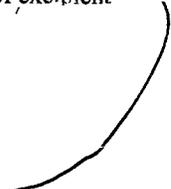
Please refer to your December 22, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for desvenlafaxine succinate tablets.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. [redacted] Type II DMF [redacted] has been reviewed and found to be incomplete. A letter detailing the deficiencies will be issued to their designated agent.
2. Information on the [redacted] of [redacted] has been provided for a number [redacted]. Additional information demonstrating the understanding and controls of [redacted] is needed:
 - a. Provide in the NDA characterization data for all known [redacted]
 - b. Describe the [redacted] in the drug substance as a [redacted]
 - c. Discuss the effect [redacted] form during drug product manufacturing.
 - d. The [redacted] process mapping study states that [redacted]
3. With respect to manufacturing process development:
 - a. Define control space and its relationship to design space for both critical and non-critical process parameters.
 - b. [redacted]
 - c. For each unit of operation, discuss whether the design space is independent of equipment and batch size.
 - d. [redacted]
 - e. Figures P.2.3-35 and P.2.3-36 in Quality Overall Summary (QOS) and Table 8.27 (Report 61567 in Section 3.2.P.2) appear to indicate [redacted]

- 
4. The QOS and Section 3.2.P.2 provide the raw material controls and identify a limited number of excipient suppliers.

- 
5. To facilitate evaluation of your proposal for

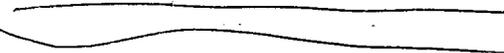
- 
6. Provide a description of the in-process sampling procedures used with non-PAT testing and explain how the sample obtained is representative of the entire batch. Where PAT testing is proposed, describe how placement of the testing device was determined and whether the measurements are representative of the entire batch.

7. The QOS and Section 3.2.P.2 provide a detailed narrative description of the product development studies and the effects of numerous variables on the manufacturing process.

- 
- 
8. As commercial experience is gained and as post-approval changes are made, the design space may change. Explain how the design space will be reassessed, verified, or redefined when a change is made in a unit of operation, process parameters, in-process controls, or when a new piece of equipment is introduced. Discuss a regulatory strategy for managing changes in design space, including expanding and contracting the design space, for critical and/or non-critical parameters.
9. Provide updated stability data for the drug product and statistical analysis (or justification for its omission) to support the proposed expiration dating period.
10. Provide a schematic drawing (with dimensions) for each tablet.

In addition, we have the following responses to the questions submitted in the February 16, 2006, amendment:

Question 1:

- a. Your proposal to submit the referenced amendment 3 months prior to the PDUFA goal date is acceptable. However, as indicated during the March 8, 2006 meeting, we recommend that the amendment be submitted as early as possible so that FDA has adequate time to review its contents.
- b. The information provided is insufficient for us to address your question. Explain the design spaces, i.e., pilot, predicted, evaluated, and proposed design spaces, presented in Tables 1.1-3 through 1.1-6, and their interrelationship. Refer to our comments 3.a, 3.b, 3.c, 7, and 8, and discuss how the control space relates to the design space.
- 

Question 2: In as much as the _____ is not part of the proposed design space, we agree that _____ for the proposed _____ As recommended in the SUPAC-MR guidance, the change should be submitted as a prior approval supplement with complete supporting information. A CBE-30 submission could be justified as part of a comparability protocol. The comparability protocol can be submitted in the original application or as a prior approval supplement. The following additional CMC information should be included in the comparability protocol:

a. 

b. 

Question 3: Identify the process controls to be used at the time of approval and those that will be introduced post-approval under the PAT implementation plan. For the PAT plan we recommend that a detailed comparability protocol be provided. The protocol should address the following:

- a. A timetable for implementation and the type of submission;
- b. The identity of the analysis to be performed for each unit of operation and what properties that analysis is intended to monitor in the process material;
- c. A description of each analytical method and the identity of the PAT equipment to be used to perform the analysis;
- d. A description of the sampling procedure used for each analysis and a discussion on how the sample represents the entire batch;
- e. The test acceptance criteria and a justification that it is suitable for the intended use;
- f. A description of the equipment training procedure;
- g. An explanation of how the analysis relates to or replaces a product release test attribute; and
- h. How future changes to any of these PAT analyses will be qualified and reported.

If you have any questions, call Amy Bertha, Regulatory Health Project Manager, at 301-796-1647.

Sincerely,

{See appended electronic signature page}

Chi-wan Chen, Ph.D.
Deputy Director
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Chi Wan Chen

5/5/2006 04:49:41 PM

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-992 Supplement # Efficacy Supplement Type SE-

Trade Name:
Established Name: Desvenlafaxine
Strengths: 100mg and 200mg

Applicant: Wyeth
Agent for Applicant:

Date of Application: December 22, 2005
Date of Receipt: December 22, 2005
Date clock started after UN:
Date of Filing Meeting: February 13, 2006
Filing Date: February 17, 2006
Action Goal Date (optional): October 22, 2006 User Fee Goal Date: October 22, 2006

Indication(s) requested: Major Depressive Disorder

Type of Original NDA: (b)(1) X (b)(2)
OR
Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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). If the application is a (b)(2), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

NDA is a (b)(1) application OR NDA is a (b)(2) application

Therapeutic Classification: S X P 2020100
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 1
Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted: YES X NO

User Fee Status: Paid X Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling.

Version: 12/15/2004

This is a locked document. If you need to add a comment where there is no field to do so, unlock the document using the following procedure. Click the 'View' tab; drag the cursor down to 'Toolbars'; click on 'Forms.' On the forms toolbar, click the lock/unlock icon (looks like a padlock). This will allow you to insert text outside the provided fields. The form must then be relocked to permit tabbing through the fields.

If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES NO X
If yes, explain:

- Does another drug have orphan drug exclusivity for the same indication? YES NO X

- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES NO

- Does the submission contain an accurate comprehensive index? YES X NO

- Was form 356h included with an authorized signature? YES X NO
If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES X NO
If no, explain:

- If an electronic NDA, does it follow the Guidance? N/A YES X NO
If an electronic NDA, all forms and certifications must be in paper and require a signature.
Which parts of the application were submitted in electronic format?

Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A YES X NO

- Is it an electronic CTD (eCTD)? N/A YES X NO
If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES X NO

- Exclusivity requested? YES, _____ Years NO X
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

- Correctly worded Debarment Certification included with authorized signature? YES X NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge"

- Financial Disclosure forms included with authorized signature? YES X NO
(Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section)? Y X NO
- PDUFA and Action Goal dates correct in COMIS? YES X NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: 64,552
- End-of-Phase 2 Meeting(s) Date(s) _____ NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s) Date(s) _____ NO
If yes, distribute minutes before filing meeting.

Project Management

- Was electronic "Content of Labeling" submitted? YES X NO
If no, request in 74-day letter.
- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES X NO
- Risk Management Plan consulted to ODS/IO? N/A X YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A X YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A X YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS DSRCS? N/A X YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to Florian Zielinski (HFD-357)? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: 2/13/06

BACKGROUND: New NME

ATTENDEES:

ASSIGNED REVIEWERS (including those not present at filing meeting) :

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Robert Levin, M.D.
Secondary Medical:	
Statistical:	Fanhui Kong
Pharmacology:	Linda Fossom
Statistical Pharmacology:	
Chemistry:	Tom Oliver, Terrence Ocheltree, William Adams
Environmental Assessment (if needed):	
Biopharmaceutical:	Kofi Kumi
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	Andrea Slavin
Regulatory Project Management:	Renmeet Gujral/ William Bender
Other Consults:	CAC consult

Per reviewers, are all parts in English or English translation? YES X NO
If no, explain:

CLINICAL FILE X REFUSE TO FILE

• Clinical site inspection needed? YES X NO

• Advisory Committee Meeting needed? YES, date if known September 7 NO

• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A X YES NO

CLINICAL MICROBIOLOGY N/A X FILE REFUSE TO FILE

STATISTICS N/A FILE X REFUSE TO FILE

BIOPHARMACEUTICS FILE X REFUSE TO FILE

• Biopharm. inspection needed? YES NO

PHARMACOLOGY N/A FILE X REFUSE TO FILE

- GLP inspection needed?

YES NO

CHEMISTRY

FILE X

REFUSE TO FILE

- Establishment(s) ready for inspection?
- Microbiology

YES NO

YES NO

ELECTRONIC SUBMISSION:
Any comments: ECTD formait

REGULATORY CONCLUSIONS/DEFICIENCIES:
(Refer to 21 CFR 314.101(d) for filing requirements.)

- The application is unsuitable for filing. Explain why:
- X The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
- No filing issues have been identified.
- Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

- 1.X If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
- 3.X Convey document filing issues/no filing issues to applicant by Day 74.

Renmeet Gujral, Pharm.D.
Regulatory Project Manager, HFD-130

Appendix A to NDA Regulatory Filing Review

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

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) 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.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

**Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):
3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," skip to question 4. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

4. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," skip to question 5. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

NOTE: *If there is more than one pharmaceutical alternative approved, consult the Director, Division of*

Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product? YES NO

If "No," skip to question 6.

If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.

- (b) Is the approved drug product cited as the listed drug? YES NO
6. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").
7. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)).) YES NO
8. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9)). YES NO
9. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES NO
10. Are there certifications for each of the patents listed for the listed drug(s)? YES NO
11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):

- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)
Patent number(s):

NOTE: IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)].

- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):
- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).
Patent number(s):
- Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?
YES NO
- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?
YES NO
- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?
N/A YES NO
- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).)?
N/A YES NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a). YES NO

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval. YES NO

- EITHER

The number of the applicant's IND under which the studies essential to approval were conducted.

IND# _____ NO

OR

A certification that the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

YES NO

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES NO

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

/s/

Renmeet Gujral
3/1/2006 02:52:34 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-992

Wyeth Pharmaceuticals, Inc.
Attention: Kenneth Bonk
Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101

Dear Mr. Bonk:

Please refer to your new drug application (NDA) dated and received December 22, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Desvenlafaxine 100mg and 200 mg tablets.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on February 17, 2006, in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Renmeet Gujral, Regulatory Project Manager, at (301) 796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**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
2/24/2006 06:04:47 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-992
IND 64,816

Wyeth Pharmaceuticals
Attention: T.G. Venkateshwaran
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Venkateshwaran:

Please refer to your Investigational New Drug Application (IND) and New Drug Application (NDA) for desvenlafaxine succinate sustained-release tablet.

We also refer to your February 1, 2006, correspondence, received February 2, 2006, requesting a meeting to discuss the application of PAT technologies for this product.

Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type C meeting as described in our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDUFA Products* (February 2000). The meeting is scheduled for:

Date: March 8, 2006

Time: 1:00 pm – 2:00 pm

Location: Food and Drug Administration

White Oak CDER Building #22 Room 1419

10903 New Hampshire Ave

Silver Spring, MD 20993-0002

CDER invited participants:

OFFICE OF NEW DRUG QUALITY ASSESSEMENT

Moheb Nasr, Director

Chi-wan Chen, Deputy Director

Ramesh Sood, Branch Chief, Division of Pre-Marketing Assessment I

Thomas Oliver, Team Leader, Division of Pre-Marketing Assessment I

Mike Adams, Chemist, Division of Pre-Marketing Assessment III

Terrance Ocheltree, Chemist, Manufacturing Science

Michael Folkendt, Supervisory Project Manager

Amy Bertha; Regulatory Health Project Manager

OFFICE OF COMPLIANCE
Division of Manufacturing and Product Quality
Nicholas Buhay, Director
Albinus D Sa, Consumer Safety Officer

OFFICE OF REGULATORY AFFAIRS
Myriam Sosa, Field Investigator

OFFICE OF NEW DRUGS
Division of Psychiatry Products
Thomas Laughren, Director
Robert Levin, Medical Officer
Renmeet Gujral, Regulatory Health Project Manager

Please have all attendees bring photo identification and allow 15-30 minutes to complete security clearance. If there are additional attendees, email that information to me at amy.bertha@fda.hhs.gov so that I can give the security staff time to prepare temporary badges in advance. Upon arrival at FDA, give the guards my number to request an escort to the conference room: (301) 796-1647.

If you have any questions, call me, at (301) 796-1647.

Sincerely,

{See appended electronic signature page}

Amy Bertha
Regulatory Health Project Manager
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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

/s/

Amy Bertha
2/16/2006 05:35:14 PM