CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-104

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

1.3.5.2 Patent Certification

The patent certifications are provided on the following pages for the patents listed in the Electronic Orange Book which was updated November 7, 2006.

Paragraph III Certification
regarding U.S. Patent No. 4,535,186
listed in the Orange Book for Effexor XR®
for Osmotica's venlafaxine 505(b)(2) NDA application

"Osmotica Pharmaceuticals certifies that Patent No. 4,535,186 will expire on December 13, 2007, and including pediatric exclusivity, U.S. Patent No. 4,535,186 will expire on June 13, 2008."

Mark S. Aikman, Pharm. D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp

13 Nov 06
Date

Statement pursuant to 21 C.F.R. § 314.50(i)(1)(iii)(A)
regarding U.S. Patent No. 5,916,923
listed in the Orange Book for Effexor XR®
for Osmotica's venlafaxine 505(b)(2) NDA application

Patent No 5,916,923 ("the '923 patent") is listed in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book") as claiming a method of using venlafaxine hydrochloride extended-release capsules (EFFEXOR XR®). The patent use code assigned to the '923 patent is "U-398," which is defined as "TREATMENT OF GENERALIZED ANXIETY DISORDER." Pursuant to § 505(b)(2)(B) of the FDC Act and FDA's implementing regulations at 21 C.F.R. § 314.50(i)(1)(iii)(A), Osmotica Pharmaceutical Corp. hereby states that the '923 method-of-use patent does not claim any of the proposed indications for which 505(b)(2) application approval is sought.

Mark S. Aikman, Pharm. D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceuticals Corp

17 Nov 06
Date

Paragraph IV Certification
regarding U.S. Patent No. 6,274,171
listed in the Orange Book for Effexor XR®
for Osmotica's venlafaxine 505(b)(2) NDA application

"Osmotica Pharmaceuticals certifies that Patent No. 6,274,171 is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of venlafaxine extended release tablets for which this application is submitted."

Mark S. Aikman, Pharm. D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp

13 Nov 06
Date

Paragraph IV Certification
regarding U.S. Patent No. 6,403,120
listed in the Orange Book for Effexor XR®
for Osmotica's venlafaxine 505(b)(2) NDA application

"Osmotica Pharmaceuticals certifies that Patent No. 6,403,120 is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of venlafaxine extended release tablets for which this application is submitted."

Mark S. Aikman, Pharm. D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp

13 Nov 06
Date

Paragraph IV Certification
regarding U.S. Patent No. 6,419,958
listed in the Orange Book for Effexor XR®
for Osmotica's venlafaxine 505(b)(2) NDA application

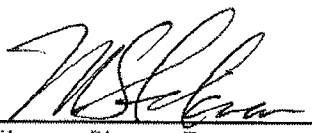
"Osmotica Pharmaceuticals certifies that Patent No. 6,419,958 is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of venlafaxine extended release tablets for which this application is submitted."

Mark S. Aikman, Pharm. D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp

13 Nov 06
Date

Paragraph IV Certification
regarding U.S. Patent No. 6,444,708
listed in the Orange Book for Effexor XR®
for Osmotica's venlafaxine 505(b)(2) NDA application

"Osmotica Pharmaceuticals certifies that Patent No. 6,444,708 is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of venlafaxine extended release tablets for which this application is submitted."



13 Nov 06

Mark S. Aikman, Pharm. D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp

Date

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 22-104 **Supplement Type (e.g. SE5):** _____ **Supplement Number:** _____

Stamp Date: December 12, 2006 **PDUFA Goal Date:** May 20, 2008

HFD 130 **Trade and generic names/dosage form:** venlafaxine hydrochloride extended release tablets

Applicant: Osmotica **Therapeutic Class:** 2020100 (antidepressant)

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

X 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): 2

Indication #1: Major Depressive Disorder (MDD) & Social Anxiety Disorder (SAD)

Is this an orphan indication?

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

X No. Please proceed to the next question.

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

☐ **Yes: Please proceed to Section A.**

X No: Please check all that apply: ____Partial Waiver ____Deferred __X__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 Aachment 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): Children and adolescents for MDD and adolescents for SAD

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.

This page was completed by:

{See appended electronic signature page}

Renmeet Grewal, Pharm.D.
Senior Regulatory Project Manager
Division of Psychiatry Products

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
5/13/2008 03:22:26 PM

1.12.10 Generic Drug Enforcement Act Statement

Osmotica Pharmaceutical Corp did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) [section 306(a) or (b)], in connection with this application.

8 Nov 08

Mark S. Aikman, Pharm.D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp

1.3.4 Financial Certification and Disclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: April 30, 2009.

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

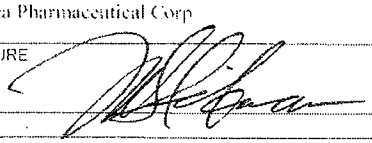
Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See attachment	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Mark S. Aikman, Pharm.D.	Vice President, Regulatory Affairs and Quality Assurance
FIRM / ORGANIZATION: Osmotica Pharmaceutical Corp	
SIGNATURE: 	DATE: 11/27/06

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (4/06)

Grewal, Renmeet

From:	Grewal, Renmeet
Sent:	Monday, May 12, 2008 2:37 PM
To:	'Mark Aikman'
Cc:	Ansah, Kofi
Subject:	NDA 22-104 RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENT

Hi Mark,

Title IX, Subtitle A, Section 901 of FDAAA amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if the Secretary determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Venlafaxine Extended Release Tablet poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Venlafaxine Extended Release Tablet. FDA has determined that Venlafaxine Extended Release Tablet is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use Venlafaxine Extended Release Tablet. Antidepressants, including venlafaxine hydrochloride, are associated with an increased risk of suicidality in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Venlafaxine Extended Release Tablet.

Therefore, we are requesting that you commit to conducting the following assessments under the specified timelines below:

1st FDAAA assessment: November 2009 (18 months from approval)
2nd FDAAA assessment: May 2011 (3 years from approval)
3rd FDAAA assessment: May 2015 (7 years from approval)

Information needed for assessment of the REMS should include but may not be limited to:

a. Survey of patients' understanding of the serious risks of Venlafaxine Extended Release Tablet
b. Report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. Report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

Given the user fee goal date of 5-20-08, we are requesting that you respond to this email no later than COB tomorrow.

Sincerely,
Rimmy

Renmeet Grewal, Pharm.D., LCDR USPHS
Regulatory Project Manager
Division of Psychiatry Products

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
5/12/2008 04:18:46 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-104

Osmotica Pharmaceutical Corporation
Attention: Mark Aikman, Vice President
Regulatory Affairs and Quality Assurance
1205 Culbreth Drive, Suite 200
Wilmington, NC 28405

Dear Mr. Aikman:

We acknowledge receipt on December 28, 2007 of your December 28, 2007 resubmission to your new drug application for Venlafaxine Hydrochloride Extended-release 37.5mg, 75mg, 150mg, and 225mg tablets.

We consider this a complete, class 1 response to our October 4, 2007 action letter. Therefore, the user fee goal date is February 28, 2008.

If you have any question, call me at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

CDR William Bender
Division of Psychiatry Products
Office of Drug Evaluation 1
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/

William Bender
1/29/2008 01:56:44 PM

Bender, William

From: Bender, William
Sent: Monday, March 12, 2007 3:24 PM
To: 'Tim Davis'
Subject: FW: NDA 22-104
Attachments: nda22104bioresponse.pdf

Attached are the comments regarding NDA 22-104 protocol for the multi-dose study.

Thank you,

William H. Bender
LCDR, USPHS
Regulatory Health Project Manager, FDA/CDER/DPP
Phone: 301-796-2145
william.bender@fda.hhs.gov

From: Bender, William
Sent: Monday, March 12, 2007 12:43 PM
To: 'Tim Davis'
Subject: RE: NDA 22-104

Hi Tim,

I should have something by early this week.

Thanks,
Bill

From: Tim Davis [mailto:davis@osmotica.com]
Sent: Thursday, March 08, 2007 11:26 AM
To: Bender, William; Mark Aikman
Subject: RE: NDA 22-104

Hi Dr. Bender,

Did OCPB indicate how long it will take to review and provide comments?

Tim

From: Bender, William [mailto:William.Bender2@fda.hhs.gov]
Sent: Thursday, March 08, 2007 11:05 AM
To: Mark Aikman
Cc: Tim Davis
Subject: RE: NDA 22-104

Hi Guys,

After OCPB reviews your draft protocol, you should submit the official protocol to your IND (71,288) and the data after the study to your NDA (22-104).

Please feel free to contact me with any questions,

Thanks,
Bill

From: Mark Aikman [mailto:aikman@osmotica.com]
Sent: Thursday, March 01, 2007 12:27 PM
To: Bender, William
Cc: Tim Davis
Subject: NDA 22-104

Mr. Bender,

In NDA 22-104, the manufacturing site listed is [redacted] located in [redacted] provides contract manufacturing services to Osmotica. As you may be aware, [redacted] is in the process of being acquired by [redacted] For Osmotica, this introduces unknown variables in that we are uncertain of how this merger will affect our product supply capabilities. It is for that reason that the application includes two comparability protocols. One protocol is for an alternate manufacturing site and one for an alternate API supplier. To assure that we do not have potential issues, we have initiated the transfer of the production to [redacted] to be the alternate site using API from an alternate supplier. Our request, if possible, is that the Agency provide to Osmotica feedback on the comparability protocols as soon as possible so that we may have this feedback prior to the initiation of the production of registration batches. Please contact Tim Davis or me if there are any questions.

b(4)

Regards,
Mark

Mark S. Aikman, Pharm.D.
Vice President, Regulatory Affairs and Quality Assurance
Osmotica Pharmaceutical Corp.
1205 Culbreth Dr., Suite 200
Wilmington, NC 28405
office (910) 509-0114
mobile (910) 200-5971

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-104

Osmotica Pharmaceutical Corporation
Attention: Timothy Davis, Manager of Regulatory Affairs
1205 Culbreth Drive
Suite 200
Wilmington, NC 28405

Dear Dr. Davis:

Please refer to your December 11, 2006 new drug application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Venlafaxine Hydrochloride Extended-Release 37.5 mg, 75 mg, 150 mg, and 225 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 as of February 10, 2007 in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues some of which have now been addressed:

Physician's Labeling Rule (PLR)

We note that your original application did not address the PLR requirements. However, we acknowledge receipt of your amendment dated January 31, 2007, providing for required PLR formatted labeling. This submission will be reviewed during the review cycle.

Labeling

[redacted] venlafaxine hydrochloride is listed on the label [e.g., the 37.5 mg bottle label lists venlafaxine hydrochloride, [redacted] The strength will need to correspond to the established name. b(4)

Clinical Pharmacology Study

Reference is also made to our teleconference held on January 31, 2007, regarding the steady-state study that you agreed to perform for this review cycle. We note your commitment to conduct this study and provide the results to the Agency by June 30, 2007.

We are providing the above comments to give you preliminary notice of potential 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. Issues may be added, deleted, expanded upon, or modified as we review the application.

If you have any questions, call LCDR William Bender, Regulatory Project Manager, at (301) 796-2145.

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
2/21/2007 03:03:42 PM

Bender, William

From: Bender, William
Sent: Friday, February 09, 2007 10:55 AM
To: 'Tim Davis'; 'Mark Aikman'
Subject: RE: Venlafaxine Hydrochloride NDA 022104

Good Morning Dr. Davis,

We did receive your revised label in the PLR format, and I also forwarded you our meeting minutes from our 1-31-07 teleconference. Your submission for NDA 22-104, venlafaxine HCL ER tablets is filable with issues. An official "filable" letter with comments will be forthcoming.

If you have any questions, please feel free to contact me.

Thank you,

William H. Bender
LCDR, USPHS
Regulatory Health Project Manager, FDA/CDER/DPP
Phone: 301-796-2145
william.bender@fda.hhs.gov

From: Tim Davis [mailto:davis@osmotica.com]
Sent: Friday, February 09, 2007 9:26 AM
To: Bender, William
Subject: Venlafaxine Hydrochloride NDA 022104

Hi Dr. Bender,

I wanted to confirm whether you received the amendment containing the revised label in the PLR format. Also, will the NDA be filed today? If you have any questions please give me a call at 910.509.0114.

Thank you,
Tim

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

/s/

William Bender
2/9/2007 11:01:23 AM
CSO

Bender, William

From: Bender, William
Sent: Thursday, February 08, 2007 1:16 PM
To: 'Mark Aikman'; 'Tim Davis'
Subject: Meeting Minutes from our 1-31-07 teleconference

Attachments: NDA 22-104 mm1-31-07 draft with OCP edits.pdf

Good Afternoon Guys,

Attached are our meeting minutes from our 1-31-07 teleconference regarding filing issues for NDA 22-104 venlafaxine hcl extended-release tablets.

If you have any questions, please feel free to contact me.

Thank you,

William H. Bender
LCDR, USPHS
Regulatory Health Project Manager, FDA/CDER/DPP
Phone: 301-796-2145
william.bender@fda.hhs.gov

NDA 22-104
ım1-31-07 draft wit.

MEMORANDUM OF MEETING MINUTES

MEETING DATE:	January 31, 2007
TIME:	4:00pm to 5:00pm
LOCATION:	Teleconference
APPLICATION:	NDA 22-104
DRUG NAME:	Venlafaxine Hydrochloride Extended-Release Tablets
SPONSOR:	Osmotica Pharmaceutical Corporation

MEETING RECORDER: Bill Bender, R.Ph. Regulatory Project Manager

FDA ATTENDEES: (Title and Office/Division)

Thomas Laughren, M.D., Division Director
Mitchell Mathis, M.D., Deputy Division Director
Raman Baweja, Ph.D., OCP Team Leader
Ronald Kavanagh, B.S. Pharm, Pharm.D., Ph.D., OCP Reviewer

EXTERNAL CONSTITUENT ATTENDEES:

Mark Aikman, Vice President of Regulatory Affairs and Quality Assurance (Osmotica)
Glenn Meyer, Chief Scientific Officer (Osmotica)
Tim Davis, Manager of Regulatory Affairs b(4)

The purpose of this teleconference was to inform the sponsor of filing issues regarding their NDA 22-104 (receipt date of 12-12-06), venlafaxine HCL ER tablets for the treatment of major depressive disorder, social anxiety disorder b(4)

The sponsor was advised of the following:

A steady-state pharmacokinetic two-way crossover comparability study of the highest proposed strength of the test product (225 mg) compared to the reference product (150 mg + 75 mg) will be needed.

The study may employ a titration phase followed by multiple dosing at the highest dose level until steady-state is achieved.

The study should be conducted under fed conditions. Comparisons under fasting conditions are not necessary.

Sample size estimates may be based on power analysis from single dose studies. (The sponsor indicated they may make adjustments to sample size for anticipated drop-outs.)

Venlafaxine (V), O-Desmethylvenlafaxine (ODV), and total active species (V + ODV) are to be assessed.

Geometric mean ratios and 90% confidence intervals should be calculated for V, ODV, and (V + ODV).

If the study report is submitted by June 30th 2007, OCP will assure that the study is reviewed during the present review cycle.

The sponsor was also advised that if they wish to submit a protocol for review, OCP will prioritize the review and provide comments as quickly as possible. In addition, the sponsor agreed to submit this multiple dose study by the end of June, 2007.

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/s/

William Bender
2/8/2007 01:24:48 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-104

INFORMATION REQUEST LETTER

Osmotica Pharmaceutical
Attention: Mark S. Aikman, Pharm.D.
VP Regulatory Affairs and Quality Assurance
1205 Culbreth Drive
Suite 200
Wilmington, NC 28405

Dear Dr. Aikman:

Please refer to your December 11, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Venlafaxine Hydrochloride Extended Release Tablets, 37.5 mg, 75mg, 150 mg, 225 mg.

We are reviewing the Chemistry, Manufacturing and Controls (CMC) 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. The specification for the drug substance does not include an acceptance criterion for controlling the drug substance particle size. Please update the drug substance specification to include [redacted] acceptance criteria for the particle size or provide a justification as to why it should be omitted. b(4)
2. Please provide validation for the following methods used to test the drug substance or confirm that these methods are identical to the methods used to test the drug product: water, related substance, residual solvents and assay.
3. Please provide all relevant information pertaining to your drug product reference standard including the batch number, manufacturing date, method of manufacture and a certificate of analysis.
4. Please provide the release specification for the drug substance to be manufactured by [redacted] as indicated in your comparability protocol. b(4)
5. Please provide in-process control limits for the depth, size and position of the hole which is laser drilled into the drug product based on the available data.
6. In your comparability protocol, you indicate that the stability protocol will employ a bracketed approach which includes placing one batch of the smallest and largest tablet count packaging size on stability; however, in the container closure section of your application you indicate that the drug product will only be packaged in one count size (i.e. 100 count). Please clarify.
7. [redacted] venlafaxine hydrochloride is listed on the label [e.g. the 37.5 mg bottle label lists venlafaxine hydrochloride, [redacted] The strength will need to correspond to the established name used on the label. b(4)
8. In an effort to obtain a full dissolution profile on stability, we recommend that you provide any additional dissolution data that you may have at various time points.

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/s/

Ramesh Sood
7/23/2007 01:49:59 PM

Bender, William

From: Bender, William
Sent: Friday, January 26, 2007 11:16 AM
To: 'Tim Davis'
Subject: NDA 22-104

Good Morning Dr. Davis,

As discussed in our telephone conversation, any labeling for an application submitted after June 30,2006 must be in PLR format. Your NDA 22,104 submission (venlafaxine HCL extended release tablets) was not in the required PLR format. This could be a potential filing issue. As promised, attached is a the web site pertaining to PLR labeling.

http://www.fda.gov/cder/regulatory/physLabel/default.htm.

Also, as promised is the dial in number for our teleconference scheduled for Wednesday, January 31, 2007 from 4:00pm to 5:00pm.

Dial in number: 866-771-7462
Passcode: 4341880

Please feel free to call me with any questions,
William H. Bender
LCDR, USPHS
Regulatory Health Project Manager, FDA/CDER/DPP
Phone: 301-796-2145
william.bender@fda.hhs.gov

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/s/

William Bender
1/26/2007 11:21:57 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-104

NDA ACKNOWLEDGMENT

Osmotica Pharmaceutical Corp.
Attention: Timothy W. Davis, Manager, Regulatory Affairs
1205 Culbreth Drive
Suite 200
Wilmington, NC 28405

Dear Mr. Davis:

We have received your new drug application (NDA) submitted under section 505(b)2 of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Venlafaxine Hydrochloride Extended-Release Tablets, 37.5mg, 75mg, 150mg, and 225mg

Review Priority Classification: Standard (S)

Date of Application: December 11, 2006

Date of Receipt: December 12, 2006

Our Reference Number: NDA 22-104

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 9, 2007 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 12, 2007.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not submitted any information regarding pediatric studies with this application. Please amend your application to address this issue.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

If you have any questions, call me at (301) 796-2145.

Sincerely,

{See appended electronic signature page}

LCDR Bill Bender, R.Ph.
Senior Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

William Bender
1/4/2007 01:43:09 PM

NDA REGULATORY FILING REVIEW

(Including Memo of Filing Meeting)

NDA # 22-104 Supplement # Efficacy Supplement Type SE-

Proprietary Name:
Established Name: Venlafaxine Hydrochloride extended-release tablets
Strengths: 37.5mg, 75mg, 150mg, and 225mg

Applicant: Osmotica Pharmaceutical Corp.
Agent for Applicant (if applicable):

Date of Application: December 11, 2006
Date of Receipt: December 12, 2006
Date clock started after UN:
Date of Filing Meeting: January 25, 2007
Filing Date: February 23, 2007
Action Goal Date (optional): October 12, 2007 User Fee Goal Date: October 12, 2007

Indication(s) requested: Treatment of major depressive disorder, social anxiety disorder, ——— b(4)

Type of Original NDA: (b)(1) ☐ (b)(2) X
AND (if applicable)
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 or efficacy supplement is a (b)(2), complete Appendix B.

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

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

User Fee Status: Paid ☐ Exempt (orphan, government) X505b2
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 by contacting the User Fee staff in the Office of Regulatory Policy. 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 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. 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 any approved (b)(1) or (b)(2) application? YES ☐ NO ☐
  If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- 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 X
  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 ☐
  If no, explain:

- 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:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES ☐

2. This application is an eNDA or combined paper + eNDA YES ☐
   This application is: All electronic X Combined paper + eNDA ☐
   This application is in: NDA format ☐ CTD format ☐
   Combined NDA and CTD formats ☐

   Does the eNDA, follow the guidance?
   (http://www.fda.gov/cder/guidance/2353fnl.pdf) YES NO ☐

   If an eNDA, all forms and certifications must be in paper and require a signature.

   If combined paper + eNDA, which parts of the application were submitted in electronic format?

   Additional comments:

3. This application is an eCTD NDA. YES X
   If an eCTD NDA, 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 . . . ."

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included?
YES ☐ NO X

- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES X NO ☐

- Is this submission a partial or complete response to a pediatric Written Request? YES ☐ NO X

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES X NO ☐
(Forms 3454 and/or 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) YES ☐ NO ☐

- PDUFA and Action Goal dates correct in tracking system? 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: 71,288

- Are the trade, established/proper, and applicant names correct in COMIS? YES X NO ☐
If no, have the Document Room make the corrections.

- End-of-Phase 2 Meeting(s)? Date(s) _____ NO X
If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) _____ NO X
If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) _____ NO X
  If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES X NO ☐
  If no, request in 74-day letter.

- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
  Was the PI submitted in PLR format? YES X NO ☐

  If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:

- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES ☐ NO X

- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES ☐ NO X

- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
  N/A X YES ☐ NO ☐

- Risk Management Plan consulted to OSE/IO? N/A X YES ☐ NO ☐

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA X YES ☐ NO ☐

If Rx-to-OTC Switch or OTC application:

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES ☐ NO ☐

- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? 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 X NO ☐
  If no, did applicant submit a complete environmental assessment? YES ☐ NO ☐
  If EA submitted, consulted to EA officer, OPS? YES ☐ NO ☐

- Establishment Evaluation Request (EER) submitted to DMPQ? YES ☐ NO X

- If a parenteral product, consulted to Microbiology Team? YES ☐ NO X

ATTACHMENT

MEMO OF FILING MEETING

DATE: February 9, 2007

NDA #: 22-104

DRUG NAMES: Venlafaxine Hydrochloride extended-release tablets

APPLICANT: Osmotica Pharmaceuticals

BACKGROUND:
(Provide a brief background of the drug, (e.g., molecular entity is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES:

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

Discipline/Organization	**Reviewer**
Medical:	Gregory Dubitsky, M.D.
Secondary Medical:	
Statistical:	
Pharmacology:	Linda Fossom
Statistical Pharmacology:	
Chemistry:	Sherita McLamore
Environmental Assessment (if needed):	
Biopharmaceutical:	Ronald Kavanagh
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	CT Viswanathan
OPS:	
Regulatory Project Management:	LCDR Bill Bender
Other Consults:	

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

CLINICAL FILE X REFUSE TO FILE ☐

- Clinical site audit(s) needed? YES X NO ☐
  If no, explain:
- Advisory Committee Meeting needed? YES, date if known _____ NO X

- 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	X	FILE	☐	REFUSE TO FILE	☐
BIOPHARMACEUTICS			FILE	X	REFUSE TO FILE	☐
• Biopharm. study site audits(s) needed? YES					☐ NO	☐
PHARMACOLOGY/TOX	N/A	☐	FILE	X	REFUSE TO FILE	☐
• GLP audit needed?					YES ☐ NO	X
CHEMISTRY			FILE	X	REFUSE TO FILE	☐
• Establishment(s) ready for inspection?					YES X NO	☐
• Sterile product?					YES ☐ NO	X
If yes, was microbiology consulted for validation of sterilization?					YES ☐ NO	☐

ELECTRONIC SUBMISSION:
Any comments:

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.

X Filing issues to be communicated by Day 74. List (optional): PLR labeling and multiple dose fed study.

ACTION ITEMS:

1. ☐ Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.

2. ☐ If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.

3. ☐ 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.

4. ☐ If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)

5. ☐ Convey document filing issues/no filing issues to applicant by Day 74.

LCDR William H. Bender
Regulatory Project Manager

Appendix A to NDA Regulatory Filing Review

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original 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) 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, or
(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.)

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) 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, and.

(3) 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) 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, or

(3) 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.

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

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

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s): Effexor XR/NDA 20-699

3. Is this application for a drug that is an "old" antibiotic (as described in the draft guidance implementing the 1997 FDAMA provisions? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.)

YES ☐ NO X

*If "**Yes**," skip to question 7.*

4. Is this application for a recombinant or biologically-derived product?

YES ☐ NO X

*If "**Yes** "contact your ODE's Office of Regulatory Policy representative.*

5. The purpose of the questions below (questions 5 to 6) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval 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 X 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**," to (a) skip to question 6. Otherwise, answer part (b and (c)).*

   (b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval? YES X NO ☐

   (c) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES X NO ☐

*If "**Yes**," (c), list the pharmaceutical equivalent(s) and proceed to question 6.*

If "No," to (c) list the pharmaceutical equivalent and contact your ODE's Office of Regulatory Policy representative.
Pharmaceutical equivalent(s): Effexor XR

6. (a) Is there a pharmaceutical alternative(s) already approved? YES ☐ NO X

(*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," to (a) skip to question 7. Otherwise, answer part (b and (c)).

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval? YES ☐ NO ☐

(c) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES ☐ NO ☐

*If "**Yes**," to (c), proceed to question 7.*

***NOTE:** If there is more than one pharmaceutical alternative approved, consult your ODE's Office of Regulatory Policy representative to determine if the appropriate pharmaceutical alternatives are referenced.*

If "No," to (c), list the pharmaceutical alternative(s) and contact your ODE's Office of Regulatory Policy representative. Proceed to question 7.

Pharmaceutical alternative(s):

7. (a) Does the application rely on published literature necessary to support the proposed approval of the drug product (i.e. is the published literature necessary for the approval)? YES X NO ☐

If "No," skip to question 8. Otherwise, answer part (b).

(b) Does any of the published literature cited reference a specific (e.g. brand name) product? Note that if yes, the applicant will be required to submit patent certification for the product, see question 12.

8. 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"). This application provides for an alternative to Effexor XR.

9. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA may refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). YES ☐ NO X

10. Is the application for a duplicate of a listed drug whose only difference is that 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 may be refused for filing under 21 CFR 314.101(d)(9)). YES ☐ NO X

11. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application may be refused for filing under 21 CFR 314.101(d)(9). YES ☐ NO X

12. Are there certifications for each of the patents listed in the Orange Book for the listed drug(s) referenced by the applicant (see question #2)? (This is different from the patent declaration submitted on form FDA 3542 and 3542a.) YES X NO ☐

13. 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.)

☐ Not applicable (e.g., solely based on published literature. See question # 7

☐ 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):

X 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s): 4,535,186

X 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): 6,274,171; 6,403,120; and 6,419,958

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)]. OND will contact you to verify that this documentation was received.*

☐ 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):

☐ 21 CFR 314.50(i)(1)(ii): No relevant patents.

X 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): 5,916,923

14. Did the applicant:

- Identify which parts of the application rely on the finding of safety and effectiveness for a listed drug or published literature describing a listed drug or both? For example, pharm/tox section of application relies on finding of preclinical safety for a listed drug.

  YES X NO ☐

  If "Yes," what is the listed drug product(s) Effexor XR *and which sections of the 505(b)(2) application rely on the finding of safety and effectiveness or on published literature about that listed drug*
  Was this listed drug product(s) referenced by the applicant? (see question # 2)

  YES X NO ☐

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug(s)?

  N/A ☐ YES X NO ☐

15. (a) Is there unexpired exclusivity on this listed drug (for example, 5 year, 3 year, orphan or pediatric exclusivity)? Note: this information is available in the Orange Book.

YES ☐ NO X

If "Yes," please list:

Application No.	Product No.	Exclusivity Code	Exclusivity Expiration

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

/s/

William Bender
3/29/2007 04:01:29 PM
CSO

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]		
NDA # 22-104 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: Venlafaxine Dosage Form: extended release tablets		Applicant: Osmotica Pharmaceutical Corporation Agent for Applicant (if applicable):
RPM: Renmeet Grewal		Division: HFD-130/DPP

NDAs:	505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 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.)	Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)): 20-699 Effexor XR, Wyeth Provide a brief explanation of how this product is different from the listed drug. Osmotic tablet in which a tablet core is produced by conventional granulation and compression ☐ If no listed drug, check here and explain: **Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.** ☒ No changes ☐ Updated Date of check: **If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.** **On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.**

❖ User Fee Goal Date Action Goal Date (if different)	5/20/2008
❖ Actions	
• Proposed action	☒ AP ☐ TA ☐ AE ☐ NA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None AE 2/26/2008 AE 10/4/2007

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

❖ Promotional Materials *(accelerated approvals only)* Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance www.fda.gov/cder/guidance/2197dft.pdf). If not submitted, explain _____	☒ Received

❖ Application[2] Characteristics	
Review priority: ☒ Standard ☐ Priority Chemical classification (new NDAs only): ☐ Fast Track ☐ Rolling Review ☐ Orphan drug designation ☐ Rx-to-OTC full switch ☐ Rx-to-OTC partial switch ☐ Direct-to-OTC NDAs: Subpart H ☐ Accelerated approval (21 CFR 314.510) ☐ Restricted distribution (21 CFR 314.520) Subpart I ☐ Approval based on animal studies BLAs: Subpart E ☐ Accelerated approval (21 CFR 601.41) ☐ Restricted distribution (21 CFR 601.42) Subpart H ☐ Approval based on animal studies ☐ Submitted in response to a PMR ☐ Submitted in response to a PMC Comments: _____	
❖ Date reviewed by PeRC *(required for approvals only)* If PeRC review not necessary, explain: _____	5/13/2008
❖ BLAs only: *RMS-BLA Product Information Sheet for TBP* has been completed and forwarded to OBPS/DRM *(approvals only)*	☐ Yes, date
❖ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Press Office notified of action (by OEP)	☐ Yes ☒ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

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

❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application)? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☒ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☒ Verified

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

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

  (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? ☒ Yes ☐ No

  (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 the rest of the patent questions.

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

  (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? ☐ 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? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *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*).* *If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.*	☐ Yes ☐ No
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist[3]	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s) AP 5/20/08 AE 2/26/2008 AE 10/4/2007
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Medication Guide/Patient Package Insert/Instructions for Use *(write submission/communication date at upper right of first page of each piece)*	☒ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ None

[3] Fill in blanks with dates of reviews, letters, etc.

• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date at upper right of first page of each submission)*	
• Most-recent division proposal for (only if generated after latest applicant submission)	
• Most recent applicant-proposed labeling	
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☐ RPM ☐ DMEDP ☐ DRISK ☐ DDMAC ☐ CSS ☐ Other reviews
❖ Proprietary Name • Review(s) *(indicate date(s))* • Acceptability/non-acceptability letter(s) *(indicate date(s))*	N/A
Administrative / Regulatory Documents	
❖ Administrative Reviews *(e.g., RPM Filing Review[4]/Memo of Filing Meeting) (indicate date of each review)*	Filing review 3/29/07
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents www.fda.gov/ora/compliance_ref/aip_page.html	
• Applicant in on the AIP	☐ Yes ☒ No
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatric Page *(approvals only, must be reviewed by PERC before finalized)*	☒ 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 *(include certification)*	☒ Verified, statement is acceptable
❖ Postmarketing Requirement (PMR) Studies	☐ None
• Outgoing communications *(if located elsewhere in package, state where located)*	In AP ltr
• Incoming submissions/communications	5/19/2008
❖ Postmarketing Commitment (PMC) Studies	☐ None
• Outgoing Agency request for postmarketing commitments *(if located elsewhere in package, state where located)*	In AP ltr

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

• Incoming submission documenting commitment	3/19/08
❖ Outgoing communications *(letters (except previous action letters), emails, faxes, telecons)*	included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• PeRC *(indicate date; approvals only)*	☐ Not applicable
• Pre-Approval Safety Conference *(indicate date; approvals only)*	☒ Not applicable
• Regulatory Briefing *(indicate date)*	☒ No mtg
• Pre-NDA/BLA meeting *(indicate date)*	☒ No mtg
• EOP2 meeting *(indicate date)*	☒ No mtg
• Other (e.g., EOP2a, CMC pilot programs)	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☐ None 5/19/08
Cross-Discipline Team Leader Review *(indicate date for each review)*	☐ None 9/26/07
Clinical Information[5]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	2/15/08, 9/26/07
• Clinical review(s) *(indicate date for each review)*	8/24/07
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Safety update review(s) *(indicate location/date if incorporated into another review)*	
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	
❖ Clinical reviews from other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ Not needed
❖ Risk Management • Review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)* • REMS Memo *(indicate date)* • REMS Document and Supporting Statement *(indicate date(s) of submission(s))*	☐ None 5/19/08
❖ DSI Clinical Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☐ None requested
Clinical Microbiology ☐ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☒ None

[5] Filing reviews should be filed with the discipline reviews.

Clinical Microbiology Review(s) *(indicate date for each review)*	☒ None
Biostatistics ☒ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☐ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ None
Statistical Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☐ None 2/11/08, 9/25/07, 3/12/07
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 2/11/08, 9/25/07, 3/12/07
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of DSI letters)*	☐ None 7/25/07
Nonclinical ☒ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☐ None
• Supervisory Review(s) *(indicate date for each review)*	☐ None
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☐ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☐ No carc
❖ ECAC/CAC report/memo of meeting	☐ None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary *(include copies of DSI letters)*	☐ None requested
CMC/Quality ☐ None	
❖ CMC/Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☐ None
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☐ None 2/28/08
• CMC/product quality review(s) *(indicate date for each review)*	☐ None 2/28/08, 10/2/07, 8/20/07
• BLAs only: Facility information review(s) *(indicate dates)*	☐ None
❖ Microbiology Reviews • NDAs: Microbiology reviews (sterility & pyrogenicity) *(indicate date of each review)* • BLAs: Sterility assurance, product quality microbiology *(indicate date of each review)*	☐ Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☐ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☐ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	
☐ Review & FONSI *(indicate date of review)*	

☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ NDAs: Methods Validation	☐ Completed ☐ Requested ☐ Not yet requested ☐ Not needed
❖ Facilities Review/Inspection	
• NDAs: Facilities inspections (include EER printout) *(date completed must be within 2 years of action date)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
• BLAs: o TBP-EER	Date completed: ☐ Acceptable ☐ Withhold recommendation
o Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) *(date completed must be within 60 days prior to AP)*	Date completed: ☐ Requested ☐ Accepted ☐ Hold

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
4/15/2009 04:27:19 PM