CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022407Orig1s000

CHEMISTRY REVIEW(S)
NDA 22-407

Facilities (EES) reviews

See pages 11-17 of proceeding Cycle 3 CMC Review
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SHANNON J CREWS
07/02/2013
NDA 22-407

VIBATIV™
(telavancin)
for injection

Theravance, Inc.

Mark R. Seggel
ONDQA/DNDQA II/Branch V

for the Division of Anti-Infective Products
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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 4

3. REVIEW DATE: 29-MAY-2013

4. REVIEWER: Mark R. Seggel

5. PREVIOUS DOCUMENTS:

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<td>Resubmission (Class 2) [eCTD 0105]</td>
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6. SUBMISSION(S) BEING REVIEWED:

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7. NAME & ADDRESS OF APPLICANT:

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<tr>
<th>Name:</th>
<th>Theravance, Inc.</th>
</tr>
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<tr>
<td>Address:</td>
<td>901 Gateway Boulevard</td>
</tr>
<tr>
<td></td>
<td>South San Francisco, CA</td>
</tr>
<tr>
<td></td>
<td>94080</td>
</tr>
<tr>
<td>Representative</td>
<td>Rebecca Coleman, Pharm.D.</td>
</tr>
<tr>
<td>Telephone:</td>
<td>650-808-6076</td>
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8. **DRUG PRODUCT NAME/CODE/TYPE:**
   
   a) Proprietary Name: VIBATIV™
   
   b) Non-Proprietary Name (USAN): telavancin hydrochloride
   
   c) Code Name/#: TD-6424
   
   d) Chem. Type/Submission Priority:
      
      - Chem. Type: 3
      - Submission Priority: S

9. **LEGAL BASIS FOR SUBMISSION:** 505(b)(1)

10. **PHARMACOL. CATEGORY:** Antibacterial

11. **DOSAGE FORM:** Sterile lyophilized powder for injection

12. **STRENGTH/POTENCY:** 250 mg per vial and 750 mg per vial

13. **ROUTE OF ADMINISTRATION:** Intravenous infusion

14. **Rx/OTC DISPENSED:** _X_Rx ___OTC

15. **SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):**
   
   _____SPOTS product – Form Completed
   
   _X____Not a SPOTS product

16. **CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:**

   (1) Vancomycin, N$_{3}$-[2-(decylamino)ethyl]-29-[[((phosphonomethyl)amino)methyl]-, monohydrochloride;

Chemistry Review Data Sheet


Molecular formula: C_{80}H_{106}Cl_{2}N_{11}O_{27}P . HCl

Molecular weight: 1755.63 (free base)

CAS-560130-42-9; CAS-372151-71-8 [telavancin].

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

See NDA 22-110 and associated reviews. See also Chemistry Reviews #1 and #2 for this NDA. No changes have been reported.

B. Other Documents:

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<td>Vibativ (telavancin) for injection; Approved 11-SEP-2009 for complicated skin and skin structure infections (eSSSI)</td>
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The Chemistry Review for NDA 22-407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 22-407, which provides for a new indication (nosocomial pneumonia) for Vibativ, relies on the applicant’s CMC documentation submitted to approved NDA 22-110. NDA 22-407 was issued a Complete Response letter on 22-Feb-2013 due to cGMP deficiencies at [REDACTED], the drug product manufacturing facility. The [REDACTED] facility has now been withdrawn from the NDA and a new drug product manufacturing facility, Hospira McPherson, Kansas has been recommended for approval (see NDA 22110/S-006 Chemistry Review #1, 29-MAY-2013).

The Office of Compliance has issued an Overall Recommendation of Acceptable for NDA 22-407 (see attached EES report).

The package insert for Vibativ approved under NDA 22-110 has been updated to reflect the additional clinical indication and to update safety information. Other minor changes to the labeling (package insert, vial label and carton) are acceptable from the chemistry, manufacturing, and controls perspective.

Overall, NDA 22-407 is recommended for approval from the chemistry, manufacturing and controls perspective.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Not Applicable

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

See NDA 22-110 and associated chemistry reviews as well as previous chemistry reviews for NDA 22-407.

B. Description of How the Drug Product is Intended to be Used
Executive Summary Section

Vibativ (telavancin) for injection is approved for the treatment of complicated skin and skin structure infections (cSSSI) under NDA 22-110. The proposed indication covers use of Vibativ for the treatment of nosocomial pneumonia (HABP/VABP).

The product is labeled for storage at 2-8°C. The current expiration dating period is 24 months.[(b)(4)]

C. Basis for Approvability or Not-Approval Recommendation

NDA 22-407, which provides for a new indication (nosocomial pneumonia) for Vibativ (telavancin) for injection, relies on the applicant’s CMC documentation submitted to approved NDA 22-110.

NDA 22-407 was issued a Complete Response letter on 22-FEB-2013, “because it [did] not meet the standards for approval under Section 505 of the Federal Food Drug & Cosmetic Act (FD&C Act). Specifically, as provided in 505(d), the Agency will refuse to approve the application if “the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity” of the product. See 21 CFR 314.110(a); 314.125(b)(1).” The Complete Response letter referred to the significant cGMP issues at the [b](d) facility.

Problems at the [b](d) facility included [b](d) issues. Telavancin for injection was voluntarily withdrawn from distribution in November 2011. On January 31, 2013, the United States District Court approved a Consent Decree of Permanent Injunction against [b](d). This decree precludes [b](d) from, among other things, manufacturing, processing, packing, labeling, holding, or distributing non-medically necessary drugs until a remediation plan has been implemented and numerous conditions are met.

In light of the cGMP issues at the [b](d) facility, Theravance identified and qualified a new drug product manufacturer, Hospira McPherson located in McPherson, Kansas. This new drug product manufacturing facility has been recommended for approval as a replacement for the problematic [b](d) facility (see NDA 22-110/S-006 Chemistry Review #1, 29-MAY-2013). [b](d) has been withdrawn as a drug product manufacturing facility (see the 27-MAR-2013 submission to NDA 22-407).

All facilities involved in the manufacture, packaging and control of Vibativ, including Hospira, have acceptable cGMP status. The Office of Compliance issued an Overall Recommendation of Acceptable for NDA 22-407 on 06-MAY-2013 (see attached EES report).

The package insert for Vibativ first approved under NDA 22-110 has been updated to reflect the additional clinical indication and to update safety information. The Description and How Supplied sections of the package insert are unaffected by addition of the new indication, although the NDCs have been revised to reflect a change in
formal product ownership. Only minor changes to reflect changes in product
ownership and NDC have been made to the vial label and carton. Based on
recommendations from DMEPA, minor changes to the Preparation and Administration
section have been made in order to minimize foaming that may occur during
reconstitution; this should reduce the potential for dosing errors. Overall, the updated
labeling is acceptable from the chemistry, manufacturing, and controls perspective.

III. Administrative

A. Reviewer’s Signature

[see electronic signature page]
Mark R. Seggel, Chemist

B. Endorsement Block

[see electronic signature page]
Rapti Madurawe, Ph.D., Branch Chief

C. CC Block

[see darrrs]
Chemistry Assessment

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data

S DRUG SUBSTANCE

See NDA 22-110 and associated reviews.

P DRUG PRODUCT

See NDA 22-110 and associated reviews.

A APPENDICES

See NDA 22-110 and associated reviews.

R REGIONAL INFORMATION

See NDA 22-110 and associated reviews.

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

Comments: The package insert has been revised to incorporate the proposed nosocomial pneumonia indication and supporting data. Other changes to the labeling (package insert, container and carton labels) have been made that reflect that Astellas is no longer involved in the marketing and distribution of Vibativ.

The revised labeling indicates that Vibativ is now a registered trademark of Theravance, Inc.; formerly the trademark was held by Astellas. The NDC numbers listed in the package insert have been changed to reflect that Astellas is no longer involved in the marketing and distribution of Vibativ.

B. Environmental Assessment Or Claim Of Categorical Exclusion

“In accordance with 21 CFR 25.31(b), Theravance, Inc., requests a categorical exclusion for an environmental assessment for Telavancin for Injection on the basis that the estimated concentrations of Telavancin at the point-of-entry into the aquatic environment will be below
1 part per billion. Theravance, Inc. does not have any knowledge of any extraordinary circumstances that that would warrant the preparation of an environmental assessment.”

**Comments:** The categorical exclusion from the preparation of an environmental assessment (EA) is acceptable based the applicant’s analysis and determination of an EIC less than 1 ppb.

### III. List Of Deficiencies To Be Communicated

Not Applicable

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**Attachment 1. EES Report**

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<td>B. SHANMUGAM Prod Qual Reviewer 3017961457</td>
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<td>K. SNOW Micro Reviewer (HFD-520) 3017960736</td>
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A GENERAL CGMP INSPECTION WAS CONDUCTED AT THIS FACILITY ON 01-APR-2009 COVERING THE LABORATORY AND QUALITY SYSTEMS. THAT INSPECTION DID NOT RESULT IN THE ISSUANCE OF A FD 483. FOUR VERBAL OBSERVATIONS WERE DISCUSSSED WITH THE FIRM. THE VERBAL OBSERVATIONS WERE REGARDING LACK OF A CAPA FOR A UV SPECTROMETER WITH A SOFTWARE PROBLEM, CHEMICAL REGENTS WERE OBSERVED TO NOT BE Labeled CORRECTLY, EXPIRED PURIFIED WATER WAS USED IN AN ANALYSIS AND IT WAS NOT NOTED BY THE REVIEWERS, AND PRE-NUMBERED WORKSHEETS ARE NOT CONTROLLED AS WELL AS THEY SHOULD BE. MANAGEMENT HAD IMPLEMENTED OR PROMISED CORRECTIVE ACTION PRIOR TO THE CLOSE OF THE INSPECTION FOR THESE ITEMS. BASED UPON THIS INSPECTION AND THE FIRM'S COMPLIANCE HISTORY, THIS FACILITY RECOMMENDS THEM AS ACCEPTABLE.

AN INSPECTION WAS CONDUCTED AT THIS FACILITY ON 06-JAN-2010 COVERING CGMS AND THIS FIRM'S ABILITY TO CONDUCT FINISHED PRODUCT AND STABILITY TESTING UNDER CONTRACT FOR VARIOUS CLIENTS. THIS INSPECTION DID NOT RESULT IN THE ISSUANCE OF A FD 483. FOUR VERBAL OBSERVATIONS WERE DISCUSSED REGARDING CGMP ISSUES. MANAGEMENT INITIATED CORRECTIVE ACTION TO THESE OBSERVATIONS PRIOR TO THE CLOSE OF THE INSPECTION. BASED UPON THIS INSPECTION AND THE FIRM'S INSPECTION HISTORY, THIS FACILITY RECOMMENDS THEM AS ACCEPTABLE.

THIS IS A NME, AS PER FACTS, THIS PARTICULAR NDA WAS NOT COVERED DURING THE
LAST INSPECTION IN (b)(4)

DO RECOMMENDATION 05-APR-2013 ACCEPTABLE MFADDEN
A CGMP INSPECTION WAS CONDUCTED FOCUSING ON THE CONTROL TESTING LABORATORY. NO FDA 483 WAS ISSUED. SEVERAL VERBAL OBSERVATIONS WERE DISCUSSED AND CORRECTED DURING THE COURSE OF THE INSPECTION. BASED UPON THE FIRM'S HISTORY AND THIS LAST INSPECTION, (b)(4) RECOMMENDS THIS FIRM AS ACCEPTABLE.

OC RECOMMENDATION 05-APR-2013 ACCEPTABLE SHARPT
DISTRICT RECOMMENDATION

Establishment: CFN: 1925202 FEI: 1925202
HOSPIRA WORLDWIDE, INC
1776 CENTENNIAL DR
MCPHERSON, KS 6746009301

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

Establishment Comment:
DRUG PRODUCT MANUFACTURER (on 04-APR-2013 by A. CUFF (HF-01) 3017904081)
Profile: SMALL VOLUME PARENTERAL, LYOPHILIZED
GAI Status: NONE

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DO RECOMMENDATION 06-MAY-2013
THE LAST EIR OF 106-10/24/12 WAS CLASSIFIED VIA F & F FOUND, PROFILE CLASS ACCEPTABLE. FARS AND DORS RECEIVED SINCE THE PREVIOUS INSPECTION DO NOT INDICATE A REASON FOR WITHHOLD BASED ON FILE REVIEW, CAN-DO RECOMMENDS APPROVABLE FOR THIS APPLICATION.

OC RECOMMENDATION 06-MAY-2013
APPLICATION ORIGINALLY FLAGGED AS AN NME THROUGH MANUAL CHECK OF PRODUCT "NME" CHECKBOX TRIGGER. THIS IS NOT AN NME.

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DO RECOMMENDATION 18-APR-2013
PROFILE CLASS CTX FOUND ACCEPTABLE. PREVIOUS THREE INSPECTIONS WERE VAI, NAI, BASED ON FILE REVIEW

OC RECOMMENDATION 18-APR-2013
PROFILE CLASS CTX FOUND ACCEPTABLE. PREVIOUS THREE INSPECTIONS WERE VAI, NAI, DISTRICT RECOMMENDATION
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Note: The Entry for 30-JUL-2012 states: "This is a NME. As per facts, this particular NDA was not covered during the last inspection in Oct 2012."

Note: The Entry for 05-APR-2013 states: "Site inspected and covered telavancin. This is not an NME, because the investigation NDA #2110 was approved and triggered surveillance coverage on 2012."
CHEMISTRY REVIEW #4

Chemistry Assessment Section

##

###

---

**OC RECOMMENDATION** 16-APR-2013

**ACCEPTABLE**

**PRABHAKAR**

SITE INSPECTED AND COVERED TELAVANCIN. THIS IS NOT AN NME, BECAUSE DISTRICT RECOMMENDATION SISTER NOA#22110 WAS APPROVED AND TRIGGERED SURVEILLANCE COVERAGE ON 2012 INSPECTION.

---

Reference ID: 3316551
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

MARK R SEGGEL
05/30/2013

RAPTI D MADURAWE
05/31/2013
NDA 22-407

VIBATIV™
(telavancin)
for injection

Theravance, Inc.

Mark R. Seggel
ONDQA/DNDQA II/Branch V

for the Division of Anti-Infective Products
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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 3

3. REVIEW DATE: 11-JAN-2013

4. REVIEWER: Mark R. Seggel

5. PREVIOUS DOCUMENTS:

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6. SUBMISSION(S) BEING REVIEWED:

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<tr>
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7. NAME & ADDRESS OF APPLICANT:

<table>
<thead>
<tr>
<th>Name:</th>
<th>Theravance, Inc.</th>
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<tbody>
<tr>
<td>Address:</td>
<td>901 Gateway Boulevard</td>
</tr>
<tr>
<td></td>
<td>South San Francisco, CA  94080</td>
</tr>
<tr>
<td>Representative:</td>
<td>Rebecca Coleman, Pharm.D.</td>
</tr>
<tr>
<td>Telephone:</td>
<td>650-808-6076</td>
</tr>
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8. DRUG PRODUCT NAME/CODE/TYPE:
Chemistry Review Data Sheet

a) Proprietary Name: VIBATIV™

b) Non-Proprietary Name (USAN): telavancin hydrochloride

c) Code Name/#: TD-6424

d) Chem. Type/Submission Priority:
   • Chem. Type: 3
   • Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Sterile lyophilized powder for injection

12. STRENGTH/POTENCY: 250 mg per vial and 750 mg per vial

13. ROUTE OF ADMINISTRATION: Intravenous infusion

14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
   _____SPOTS product – Form Completed

   _X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

(1) Vancomycin, $\beta^3$-[2-(decylamino)ethyl]-29-[(phosphonomethyl)amino]methyl]-, monohydrochloride;

(2) (3S,6R,7R,22R,23S,26S,36R,38aR)-3-(2-Amino-2-oxoethyl)-10,19-dichloro-44-[(2-\text-O}-[3-[(2-
   decylamino)ethyl]amino]-3-C-methyl-2,3,6-trideoxy-\text-O}-\text-o-hexopyranosyl]-\text-B-D-
   glucopyranosyl][oxy]-7,22,28,30,32-pentahydroxy-6-[[2(R)-4-methyl-2-(methylamino)-pentanoyl]amino]-2,5,24,38,39-pentaoxo-29-[(phosphonomethyl)amino]methyl]-2,3,4,5,6,7,23,24,25,26,36,37,38,38a-tetrahydro-23,36-
17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

See NDA 22-110 and associated reviews. See also Chemistry Reviews #1 and #2 for this NDA. No changes have been reported.

B. Other Documents:

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<td>NDA 22-110</td>
<td>Vibativ (telavancin) for injection; Approved 11-SEP-2009 for complicated skin and skin structure infections (cSSSI) (01/08)</td>
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<td>Chemistry Review #1, 30-SEP-2009</td>
<td>NDA 22-407</td>
<td>Vibativ; indicated for the treatment of nosocomial pneumonia; not approved</td>
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18. STATUS:

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<td>09-JAN-2012</td>
<td>T.Gooen, Office of Compliance</td>
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The Chemistry Review for NDA 22-407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 22-407, which provides for a new indication (nosocomial pneumonia) for Vibativ, relies on the applicant’s CMC documentation submitted to approved NDA 22-110. However, at this time NDA 22-407 is not recommended for approval due to an overall recommendation of Withhold issued by the Office of Compliance on 09-JAN-2013. This recommendation is based on the significant cGMP issues identified at the drug product manufacturing site (see attached EES report).

Labeling negotiations have not been completed at this time; labeling will be finalized (0)(4)

From the chemistry, manufacturing and controls perspective NDA 22-407 is not recommended for approval.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Not Applicable

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

See NDA 22-110 and associated chemistry reviews as well as previous chemistry reviews for NDA 22-407.

B. Description of How the Drug Product is Intended to be Used

Vibativ (telavancin) for injection is approved for the treatment of complicated skin and skin structure infections (cSSSI) under NDA 22-110. The proposed indication covers use of Vibativ for the treatment of nosocomial pneumonia (HABP/VABP).

The product is labeled for storage at 2-8°C (b)(4) The current expiration dating period is (b)(4)
C. Basis for Approvability or Not-Approval Recommendation

Significant cGMP issues have been identified affecting a range of sterile intravenous products. Problems include [b] Telavancin for injection was [voluntarily] withdrawn from distribution in November 2011.

The Office of Compliance issued an overall recommendation of Withhold for this application on 09-JAN-2013 (see attached EES report). Therefore this application cannot be approved from the CMC perspective.

III. Administrative

A. Reviewer’s Signature

{see electronic signature page}
Mark R. Seggel, Chemist

B. Endorsement Block

{see electronic signature page}
Rapti Madurawe, Ph.D., Branch Chief

C. CC Block

{see darrts}
Chemistry Assessment

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data

S DRUG SUBSTANCE

See NDA 22-110 and associated reviews.

P DRUG PRODUCT

See NDA 22-110 and associated reviews.

A APPENDICES

See NDA 22-110 and associated reviews.

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

Comments: The package insert has been revised to incorporate the proposed nosocomial pneumonia indication and supporting data. Other changes to the labeling (package insert, container and carton labels) have been made that reflect that Astellas is no longer involved in the marketing and distribution of Vibativ. Labeling negotiations will be completed under NDA 22-110.

The revised labeling indicates that Vibativ is a registered trademark of Theravance, Inc. However, this is not currently reflected in the uspto.gov database, which indicates that the trademark is still registered to Astellas.

The NDC numbers listed in the package insert have been changed, presumably to reflect that Astellas is no longer involved in the marketing and distribution of Vibativ. However, the FDA’s NDC directory only links Vibativ with the previous Astellas NDC numbers.
B. Environmental Assessment Or Claim Of Categorical Exclusion

“In accordance with 21 CFR 25.31(b), Theravance, Inc., requests a categorical exclusion for an environmental assessment for Telavancin for Injection on the basis that the estimated concentrations of Telavancin at the point-of-entry into the aquatic environment will be below 1 part per billion. Theravance, Inc. does not have any knowledge of any extraordinary circumstances that that would warrant the preparation of an environmental assessment.”

*Comments: The categorical exclusion from the preparation of an environmental assessment (EA) is acceptable based the applicant’s analysis and determination of an EIC less than 1 ppb.*

III. List Of Deficiencies To Be Communicated

Not Applicable
Attachment 1. EES Report

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application:
NDA 224677/000

Firm Date:
26-JUN-2019

Regulatory:
12-JAN-2019

Applicant:
THERAVANCE INC
981 GATEWAY BLVD
SOUTHWAY SAN FRANCISCO, CA 94080

Brand Name:
VIBATIV

Establish:

Generic Name:

Priority:

Product Number:

Dosage Form:

Ingredient:

Strength:

Org. Code:
520

DEN: POWDER, FOR INJECTION SOLUTION. LYSOPHILIZED.
TEFLAONE HYDROCHLORIDE. 30MG
DEN: POWDER, FOR INJECTION SOLUTION. LYSOPHILIZED.
TEFLAONE HYDROCHLORIDE. 75MG

Application Comment:

FDA Contact:
A. CUFF
Project Manager
(HF-01)
5017944581

M. HANDBUSCH
Review Chemist
5017944457

R. MADARIAGA
Team Leader
5017944468

Overall Recommendation:
WITHHOLD

on 03-JAN-2011

by T. GOGGEN

(WF-320)

3017943257

WITHHOLD

on 12-JUL-2011

by EES_PED

ACCEPTABLE

on 13-FEB-2011

by EES_PED

ACCEPTABLE

on 12-JAN-2012

by EES_PED

DMF No:
AAAD: N 922119

Responsibilities:
FINISHED DOSAGE MANUFACTURER

Establishment Comment:
DRUG PRODUCT MANUFACTURING, RELEASE TESTING, PACKAGING AND LABELING. DATA BRANCED TO THIS FACILITY. (08-03-2009 TO 30-JUN-2009) (02-MAR-2008 TO 30-JUN-2008)

Profile:
SMALL VOLUME INTRAVENOUS, LYSOPHILIZED

FM Status:
POTENTIAL DM

Mission Name Mission Date Request Type Planned Completion Decision

SUBMITTED TO OCC 23-MAR-2009

SUBMITTED TO DO

23-MAR-2009 Product Specific

FLOORS

DO RECOMMENDATION

23-JUN-2009

PENDING

ACCEPTABLE

KUOLVER

BASED ON FILE REVIEW

OC RECOMMENDATION

23-JUN-2009 ACCEPTABLE

PERMISSIBLE

DISTRICT RECOMMENDATION

SUBMITTED TO OCC 23-DEC-2009

SUBMITTED TO DO

24-DEC-2009 Product Specific

FLOORS

DO RECOMMENDATION

10-FEB-2010

ACCEPTABLE

KUOLVER

BASED ON FILE REVIEW

OC RECOMMENDATION

10-FEB-2010

ACCEPTABLE

PERMISSIBLE

DISTRICT RECOMMENDATION

SUBMITTED TO OCC

30-JUL-2012

SUBMITTED TO DO

30-JUL-2012 90-Day Letter

DAY

DO RECOMMENDATION

19-SEP-2012

WITHHOLD

PENDING REGULATORY ACTION WITH

OC RECOMMENDATION

08-JAN-2013

WITHHOLD

TODD

WARNING LETTER ISSUED

Reason

SUBMITTED TO OCC

23-MAR-2009

SUBMITTED TO DO

23-MAR-2009

Product Specific

FLOORS

DO RECOMMENDATION

23-JUN-2009

PENDING

ACCEPTABLE

KUOLVER

BASED ON FILE REVIEW

OC RECOMMENDATION

23-JUN-2009

ACCEPTABLE

PERMISSIBLE

DISTRICT RECOMMENDATION

SUBMITTED TO OCC

23-DEC-2009

SUBMITTED TO DO

24-DEC-2009

Product Specific

FLOORS

DO RECOMMENDATION

10-FEB-2010

ACCEPTABLE

KUOLVER

BASED ON FILE REVIEW

OC RECOMMENDATION

10-FEB-2010

ACCEPTABLE

PERMISSIBLE

DISTRICT RECOMMENDATION

SUBMITTED TO OCC

30-JUL-2012

SUBMITTED TO DO

30-JUL-2012 90-Day Letter

DAY

DO RECOMMENDATION

19-SEP-2012

WITHHOLD

PENDING REGULATORY ACTION WITH

OC RECOMMENDATION

08-JAN-2013

WITHHOLD

TODD

WARNING LETTER ISSUED

Reference ID: 3244056
### Chemistry Assessment Section

#### Finished Dosage Stability Tester

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**DO Recommendation:** 01-Apr-2009

A general GMP inspection was conducted at this facility on 01 Apr 2009. The inspection did not result in the issuance of a 483. Four verbal observations were discussed with the firm regarding lack of a CAPA for a UV spectrometer with a software problem, chemical discrepancies, observed to not be labeled correctly, expired purified water used in an analysis, and it was not noted by the reviewers. Premises worksheets are not controlled as well as they should be. Management had not discussed or promised corrective action prior to the close of the inspection. Based upon this inspection and the firm’s compliance history, CDO recommends them as acceptable.

**OC Recommendation:** 01-Apr-2009

Acceptable. District recommendation.

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**DO Recommendation:** 06 Jan-2010

An inspection was conducted at this facility on 06 Jan 2010. During the inspection, it was observed that the firm’s ability to conduct finished product and stability testing under contract for various clients. This inspection did not result in the issuance of a 483. The firm’s worksheets are not controlled as well as they should be. Management had not discussed or promised corrective action prior to the close of the inspection. Based upon this inspection and the firm’s compliance history, CDO recommends them as acceptable.

**OC Recommendation:** 06 Jan-2010

Acceptable. District recommendation.

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**Decision:** Acceptable. District recommendation.

**Reason:** Based on profile.
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## CHEMISTRY REVIEW #3

### Chemistry Assessment Section

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Reference ID: 3244056
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARK R SEGGEL  
01/11/2013

RAPTI D MADURAWE  
01/11/2013

Reference ID: 3244056
NDA 22-407

VIBATIV™
(telavancin hydrochloride)
For Injection

Theravance, Inc.

Balajee Shanmugam, Ph.D
Division of Pre-Marketing Assessment, Branch V
ONDQA
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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 2

3. REVIEW DATE: 1-NOV-2010

4. REVIEWER: Balajee Shanmugam, Ph.D.

5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

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7. NAME & ADDRESS OF APPLICANT:

   Name: Theravance, Inc.
   Address: 901 Gateway Boulevard, South San Francisco, CA 94080.
   Representative: Rebecca Coleman, PharmD
   Telephone: 650-808-6076
8. DRUG PRODUCT NAME/CODE/TYPE:

   a) Proprietary Name: VIBATIV™
   b) Non-Proprietary Name (USAN): telavancin
   c) Code Name/# (ONDC only):
   d) Chem. Type/Submission Priority (ONDC only):
      • Chem. Type: 3
      • Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b) (1)

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Sterile lyophilized powder for injection

12. STRENGTH/POTENCY: 250 and 750 mg

13. ROUTE OF ADMINISTRATION: Intravenous infusion

14. Rx/OTC DISPENSED: __X__Rx    ____OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
    _____SPOTS product – Form Completed
    __X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

   Molecular formula: C₈₀H₁₀₆Cl₂N₁₁O₂₇P  · xHCl (where x= 1-3)
   Molecular weight: 1755.63 (free base)
   CAS: 380636-75-9
17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

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1 Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 – Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

2 Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)
The Chemistry Review for NDA 22-407

The Executive Summary

Recommendation and Conclusion on Approvability

Telavancin is a lipoglycopeptide antibiotic which in this application is indicated for the treatment of nosocomial pneumonia.

The company has cross referenced NDA 22-110 for CMC information which was previously reviewed by this reviewer and recommended Approval from Chemistry perspective. Please refer to Chemistry reviews of NDA 22-110 by this reviewer for further information.

NDA 22-407 was issued a Complete Response and the resubmission under review was submitted on 30-June-2010. There is no new CMC information in this submission. Office of Compliance had recommended Approval of the facilities on 10-Feb-2010. The EES summary report is provided below.

In accordance to 21 CFR 314.50, NDA 22-407 by way of cross-reference to NDA 22-110 provides adequate information on manufacturing and packaging procedures, in-process controls, methods, and specification. Therefore, from chemistry perspective, the application is recommended for Approval.
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/s/

BALAJEE SHANMUGAM
12/01/2010
CMCReview2

STEPHEN P MILLER
12/03/2010
I concur - this NDA is recommended for approval from the CMC perspective.
NDA 22-407

VIBATIV™
(telavancin hydrochloride)
For Injection

Theravance, Inc.

Balajee Shanmugam, Ph.D
Division of Pre-Marketing Assessment, Branch IV
ONDQA
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1. NDA 22-407

2. REVIEW #: 1

3. REVIEW DATE: 14-SEPT-2009

4. REVIEWER: Balajee Shanmugam, Ph.D.

5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

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7. NAME & ADDRESS OF APPLICANT:

   Name: Theravance, Inc.
   Address: 901 Gateway Boulevard, South San Francisco, CA 94080.
   Representative: Rebecca Coleman, PharmD
   Telephone: 650-808-6076
8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: VIBATIV™
   b) Non-Proprietary Name (USAN): telavancin
   c) Code Name/# (ONDC only):
   d) Chem. Type/Submission Priority (ONDC only):
      • Chem. Type: 3
      • Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b) (1)

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/s/

BALAJEE SHANMUGAM
09/29/2009
CMC Review

STEPHEN P MILLER
09/30/2009
I concur, as Acting Branch Chief