CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-327

CHEMISTRY REVIEW(S)

Memorandum

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

Date: May 12, 2009

From: Yichun Sun, Ph.D.
Review Chemist, ONDQA
Premarketing Assessment Division II
ONDQA

Through: Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Premarketing Assessment Division II
ONDQA

To: NDA 22-327, CMC Review #1

Subject: Establishment Evaluation

At the time of the CMC review was written, the Establishment Evaluation was pending. On May 12, 2009, the Office of Compliance gave an overall acceptable recommendation for all the facilities involved in the manufacture and test of the drug substance and drug product. Thus, this application is recommended for approval from the perspective of Chemistry, Manufacturing and Controls. This memorandum closes all pending issues for this NDA from the CMC perspective. The EER Summary Report is shown below:

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: NDA 22327/000	Sponsor: NOVARTIS CONS
Org Code: 560	1400 SOUTH ORANGE AVE
Priority: 5S	ORLANDO, FL 32806
Stamp Date: 16-JUL-2008	Brand Name: LANSOPRAZOLE
PDUFA Date: 16-MAY-2009	Estab. Name:
Action Goal:	Generic Name: LANSOPRAZOLE
District Goal: 17-MAR-2009	Dosage Form: (DELAYED RELEASE CAPSULE)
Strength: 15 MG	

FDA Contacts:	S. GOLDIE	Project Manager	301-796-2055
	M. YSERN	Review Chemist	301-796-1487
	S. DING	Team Leader	301-796-1349

Overall Recommendation: ACCEPTABLE on 12-MAY-2009
by E. JOHNSON (HFD-320) 301-796-3334

Establishment: CFN: [redacted] FEI: [redacted]

[redacted] b(4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE PACKAGER

Profile: CHG OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 20-AUG-08

Decision: ACCEPTABLE

Reason: BASED ON PROFILE

Establishment: CFN: [redacted] FEI: [redacted]

[redacted] b(4)

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

DRUG SUBSTANCE RELEASE TESTER

Profile: CSN OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 29-APR-09

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

Establishment: CFN: 1911445 FEI: 1911445

NOVARTIS CONSUMER HEALTH INC
10401 HWY 6
LINCOLN, NE 685179626

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE PACKAGER

FINISHED DOSAGE RELEASE TESTER

Profile: CHG OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 13-APR-09

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

Establishment: CFN: FEI: ———

b(4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE RELEASE TESTER

Profile: CHG OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 04-SEP-08

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

Establishment: CFN: 9616691 FEI: 3002870748

TAKEDA IRELAND LTD
BRAY BUSINESS PARK
KILRUDDERY, CO. WICKLOW, EI

DMF No: AADA:

Responsibilities: INTERMEDIATE MANUFACTURER

INTERMEDIATE RELEASE TESTER

Profile: NEC OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 12-MAY-09

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

Establishment: CFN: 9610992 FEI: 3002808311

TAKEDA PHARMACEUTICAL CO LTD
17-85 JUSO-HONMACHI 2-CHOME
YODOGAWA-KU, OSAKA, JA 532-8686

DMF No: AADA:

Responsibilities: INTERMEDIATE MANUFACTURER

INTERMEDIATE RELEASE TESTER

Profile: CRU OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 16-JAN-09

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

Establishment: CFN: 9610307 FEI: 3002808306

TAKEDA PHARMACEUTICAL COMPANY LIMITED
4720 TAKEDA MITSUI
HIKARI, JA

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

DRUG SUBSTANCE RELEASE TESTER

Profile: CSN OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 16-JAN-09

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

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

/s/

Yichun Sun
5/12/2009 06:06:33 PM
CHEMIST

Marie Kowblansky
5/12/2009 06:08:56 PM
CHEMIST
Acting Branch Chief for Moo-Jhong Rhee

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

/s/

Yichun Sun
5/12/2009 06:06:33 PM
CHEMIST

Marie Kowblansky
5/12/2009 06:08:56 PM
CHEMIST
Acting Branch Chief for Moo-Jhong Rhee

Marie Kowblansky
5/12/2009 06:11:20 PM
CHEMIST

NDA 22-327

PREVACID® 24HR (Lansoprazole) Delayed-Release Capsules

Novartis Consumer Health, Inc.

Yichun Sun, Ph.D.

Review Chemist

Branch III, Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment

CMC REVIEW OF NDA 22-327
For the Division of Nonprescription Clinical Evaluation (HFD-595)

Table of Contents

Chemistry Review Data Sheet

1. NDA: #22-327

2. REVIEW #: 1

3. REVIEW DATE: 24-March-2009

4. REVIEWER: Yichun Sun, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
IND 74,256	May 08, 2006
Pre-NDA meeting minutes	April 15, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	July 15, 2008
Amendment (BC)	November 7, 2008
Amendment (BC)	January 16, 2009
Amendment (BC)	January 19, 2009
Amendment (BL)	February 20, 2009
Amendment (BC)	March 4, 2009
Amendment (BC)	March 11, 2009

7. NAME & ADDRESS OF APPLICANT:

Name: Novartis Consumer Health, Inc.

Address: 200 Kimball Drive
Parsippany, NJ 07054-0622

Representative: Kim Stranick, Ph.D.

Telephone: (973) 503-7386

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: PREVACID®
b) Non-Proprietary Name (USAN): Lansoprazole
c) Code Name/# (ONDQA only): N/A
d) Chem. Type/Submission Priority (ONDQA only):
- Chem. Type: 5
- Submission Priority: Standard Review

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

10. PHARMACOL. CATEGORY: Proton pump inhibitors

11. DOSAGE FORM: Capsules, Delayed-Release

12. STRENGTH/POTENCY: 15 mg

13. ROUTE OF ADMINISTRATION: Oral

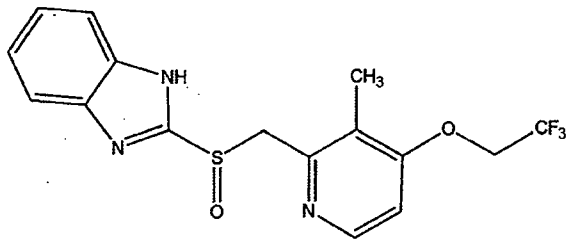
14. Rx/OTC DISPENSED: ____ Rx __X__ OTC

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:

2-[[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole



Empirical formula: $C_{16}H_{14}F_3N_3O_2S$
Molecular weight: 369.37

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE [1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA
—	III			4	NA	NA	NA

b(4)

[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)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-406	PREVACID® (lansoprazole) Delayed-Release Capsules
NDA	21-281	PREVACID® (lansoprazole) for Delayed-Release Oral Suspension
NDA	21-428	PREVACID® Solutab™ (lansoprazole) Delayed-Release Orally Disintegrating Tablets

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A	----	----
EES	Pending	----	----
Pharm/Tox	N/A	----	----
Biopharm	N/A	----	----
LNC	N/A	----	----
Methods Validation	N/A	----	----
DMET/DDMAC	N/A	----	----
EA	Categorical Exclusion Acceptable	See Review Date Above	Y. Sun
Microbiology	N/A	----	----

The Chemistry Review for NDA 22-071

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient CMC information to assure the identity, strength, purity, and quality of the drug product. Labels have adequate information as required. Therefore, from a CMC perspective, this NDA is recommended for "Approval" with pending review on Establishment Evaluation.

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

[

]

b(4)

II. Summary of Chemistry Assessments

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

Drug Substance

The drug substance, lansoprazole, used in the drug product of this NDA is the same active pharmaceutical ingredient (API) used in the following marketed drug products: PREVACID® (lansoprazole) Delayed-Release Capsules (NDA # 20-406), PREVACID® (lansoprazole) for Delayed-Release Oral Suspension (NDA # 21-281) and PREVACID® Solutab™ (lansoprazole) Delayed-Release Orally Disintegrating Tablets (NDA # 21-428). The proposed OTC lansoprazole delayed-release capsules are administered through the same administration route, oral, as the aforementioned prescription drug products. And the dose (15 mg) of the OTC drug product is lower than the higher strength (30 mg) of the these prescription drug products. Therefore, the in-process controls and specifications of the drug substance set for the these prescription drug products are adequate to ensure the identity, strength, purity and quality of the drug substance used in the proposed OTC lansoprazole delayed-release capsules. As agreed with FDA at the Pre-NDA Meeting of March 17, 2008, all the information regarding Chemistry, Manufacturing and Controls for lansoprazole drug substance is cross referenced to NDA 20-406.

Drug Product

The drug product, Prevacid® 24HR (lansoprazole) delayed-release capsules, is capsules (Size #3) filled with enteric coated granules containing 15 mg lansoprazole. The capsule shell has a pink body and teal (blue-green) cap with a black tamper evident band. The

capsule is printed with [ ] on the teal (blue-green) cap. Enteric coated lansoprazole granules, which are filled into PREVACID® (lansoprazole) Delayed-Release Capsules (NDA # 20-406), are procured from Takeda, which is the approved source under NDA 20-406. The container closure system proposed to market the OTC lansoprazole delayed-release capsules is a 14 count, [ ] bottle with child resistant [ ] cap. The proposed in-process controls and drug product specifications provide adequate assurance for the identity, strength, purity and quality of the OTC drug product. An expiration dating of 24 months is recommended for the OTC drug product stored at room temperature based on the stability data provided. The OTC lansoprazole delayed-release capsules, are proposed to be used for the treatment of frequent heartburn (occurs 2 or more days a week) in adults 18 years of age and older. This indication is consistent with the currently approved and marketed over-the-counter Proton Pump Inhibitor (PPI). One 15 mg capsule is to be taken orally once a day (every 24 hours) for 14 days. b(4)

The changes that the applicant proposed to make when switching the prescription drug product to the OTC drug product are summarized in the following Table.

Summary of Changes Made to TAP Lansoprazole Delayed-Release Capsules

Description of changes	Capsules used in pivotal studies	To-be-marketed OTC Capsules	Level defined in SUPAC IR
Capsules	Pink cap with a teal (blue-green) body	Teal (blue-green) cap with a pink body	2
Banding	No	Gelatin tamper evident band	1
Banding step in the manufacturing process	No	Yes	1
Manufacturing site	Osaka Japan	Lincoln, NE (USA) [ ]	3
Packaging configuration	30 capsules in bottles	14 capsules in [ ] bottles	NA

b(4)

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

Prevacid® 24HR (lansoprazole) delayed-release capsules are indicated for the treatment of frequent heartburn (occurs 2 or more days a week). One 15 mg capsule is to be taken orally once a day (every 24 hours) for 14 days.

C. Basis for Approvability or Not-Approval Recommendation

This NDA provided adequate information on the raw material controls, manufacturing process, specifications, and container/closure. It also provided sufficient stability data to assure identity, strength, purity and quality of the drug product during the expiration dating period. Labels have required information. However, the Establishment Evaluation for the manufacturing and testing facilities is pending. The Office of Compliance has not given an overall acceptable recommendation for all the facilities involved.

III. Administrative

A. Reviewer's Signature

/s/ Y. Sun, Ph.D.

B. Endorsement Block

Yichun Sun, Ph.D. Reviewer	Date
Shulin Ding, Ph.D. Pharmaceutical Assessment lead	Date
Moo-Jhong Rhee, Ph.D. Branch Chief	Date
Jeannie David, M.S. Project Manager	Date

C. CC Block

65 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 1

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/s/

Yichun Sun
3/24/2009 04:02:33 PM
CHEMIST

Moo-Jhong Rhee
3/25/2009 04:42:36 PM
CHEMIST
Chief, Branch III

Initial Quality Assessment
Branch III
Pre-Marketing Assessment Division II

OND Division:	Division of Nonprescription Clinical Evaluation
NDA:	22-327
Applicant:.	Novartis Consumer Health, Inc.
Stamp Date:	July 16, 2008
PDUFA Date	May 16, 2009
Trademark:	PREVACID® 24HR
Established Name:	Lansoprazole
Dosage Form:	Delayed-release Capsule
Route of Administration:	Oral
Indication:	Frequent heartburn
PAL:	Shulin Ding

	YES	NO
ONDQA Fileability:	☒	☐
Comments for 74-Day Letter	☒	☐

Summary and Critical Issues

A. Summary

This NDA is submitted by Novartis Consumer Health under section 505(b)(1) of the Federal Food Drug and Cosmetic Act in support of the nonprescription marketing of PREVACID® 24 HR (lansoprazole) 15 mg delayed release capsules for the treatment of frequent heartburn. This is not a switch of PREVACID delayed release capsules 15 mg (NDA 20-406, held by TAP Pharmaceutical Products and approved in 1995) because OTC indication is different from those approved under prescription NDA 20-406. Novartis conducted two Phase 3 and one Phase 2 clinical studies to support the proposed OTC use.

All CMC information of drug substance (lansoprazole USP), and most of CMC information of drug product are referenced to NDA 20-406. A Full-Right-of-Reference letter from TAP Pharmaceutical Products is included in this OTC NDA.

When compared with the approved Rx product, the OTC product has the following changes: (1) formulation of gelatin capsules due to color changes in capsule body/cap and the addition of a black, tamper-evident gelatin band, (2) manufacturing site for encapsulation and banding, (3) packaging site, (4) addition of banding process, and (5) packaging configurations and some packaging components. The chemistry, manufacturing and controls of the enteric film coated granules, the most important part of the drug product, remains the same. Neither is Drug product specification (tests, methods, and acceptance criteria) changed.

PREVACID® 24 HR 15 mg is a size 3 hard gelatin capsule with teal (blue-green) cap, pink body, and a black tamper-evident band. A [ ] is printed on the teal cap. The

b(4)

packaging configurations proposed for the OTC marketing are 14 counts in — white [redacted] bottle with a child-resistant closure [redacted] b(4)

The stability data supporting the proposed [redacted] expiry period at the storage of 20-25°C include long term (25°C/60% RH) data of 12 months and accelerated temperature (40°C/75% RH) data of 6 months from 2 small batches for each configuration. Results of special stability studies such as freeze/thaw and photostability are also provided in the NDA. A categorical exclusion from the requirement to prepare an Environmental Assessment is claimed for this NDA. b(4)

B. Critical issues for review

Establishments

- Address and contact information for facilities involved in the manufacturing and testing of drug substance and delayed release granules are not provided in the NDA. Although the applicant references to NDA 20-406 for drug substance and delayed release granules, the site information should be clearly stated in this NDA as a confirmation to facilitate review and inspection

Drug Product Manufacturing

- Multiple sites are involved in encapsulation, banding, and packaging. Based on the information provided in the NDA, it is possible that encapsulation/banding may be done at one site, and packing be done on another site. The applicant does not provide control information for handling, shipping, storage, and release of bulk capsules for packaging.

Drug Product Specification

- The test on related substances is not included in the proposed OTC specification. This test was included in the originally approved specification for the prescription product (NDA 20-406). It was discontinued in year 2006 after a review of stability data from 168 batches. Whether we can grant the waiver of this test for this OTC NDA with only 2-3 batches of data needs to be carefully reviewed.

- Microbiological test is proposed to be performed for the first 5 batches, and then one batch per year afterward. The reduced testing may be acceptable if the proposal is site specific. This is because three different sites are involved in encapsulation/banding and packaging. Microbiological property of a batch which is encapsulated/banded at one site can not and should not be used to represent that of the batches encapsulated/banded at a different site.

Drug Product Container/Closure Systems

- It is unclear which packaging configurations are sought for approval for OTC marketing. [redacted], the proposed label/labeling section indicates three bottle configurations (14, 28 and 42 counts). CMC review can not be properly performed without an accurate understanding of the configurations sought for approval. b(4)

Drug Product Stability

- The batch size of registration stability batches is very small [redacted] which is only 6% of the commercial batch size [redacted]. b(4)

Link between Phase 3 Clinical Batches and Commercial Batches

- The clinical supplies for the pivotal clinical studies supporting this NDA were white, opaque, non-banded capsules manufactured by Takeda Osaka Japan. These capsules are of a different formulation from the approved prescription formulation and also different from the proposed to-be-marketed OTC formulation. Additionally, Takeda Osaka Japan is not a designated encapsulation/banding site for the commercialization of the OTC product. Neither was it a site for producing the registration stability batches. The differences in formulation, banding, and site of encapsulation/banding between Phase 3 clinical and commercial batches raise a question about the need to generate a link (e.g. in-vitro dissolution profile comparison) between Phase 3 clinical and commercial batches. The applicant does not include a comparison of dissolution profile in the NDA.

C. Comments for 74-Day Letter

The following comments are to be conveyed to the applicant in the 74-day letter:

1. Provide street address, contact information, and CFN/FEI number for each facility which involves in manufacturing/testing of drug substance and delayed-release granules.

2. Provide a statement which clearly state the to-be-marketed packaging configurations sought for approval for this NDA.

3. Provide a dissolution profile comparison with f_2 analysis for the proposed OTC capsules versus the capsules used in the clinical studies, and for the proposed OTC capsules versus the approved prescription capsules. We recommend that you use the dissolution method, NCH 1577-F-5 Tier 1, described in the NDA Module 3.2.P.5.2. Tabulated data for each capsule in both acidic and buffer stages should be submitted in addition to lot number, manufacturing information (date, site, batch size, etc.), graphic presentations of dissolution profiles, and f_2 analysis results. Inform the Agency immediately when a significant difference in dissolution profiles between study arms is noticed using Tier 1 method.

D. Comments/Recommendation

This NDA is **fileable** from chemistry, manufacturing and controls (CMC) perspective. The major review issues include drug product specification, container/closure system, stability, and dissolution comparison.

GMP inspections have been requested. The drug substance manufacturing site is in Japan and — The drug product manufacturing sites are in Japan, Ireland, — , and U.S. b(4)

Shulin Ding
Pharmaceutical Assessment Lead, Branch III

Moo-Jhong Rhee
Chief, Branch III

Filing Checklists

A. Administrative Checklists

YES	NO		Comments
x		On its face, is the section organized adequately?	
x		Is the section indexed and paginated adequately?	
x		On its face, is the section legible?	
x		Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	
x		Has an environmental assessment report or categorical exclusion been provided?	

B. Technical Checklists

1. Drug Substance: Lansoprazole USP referenced to approved NDA 20-406

	x	Does the section contain synthetic scheme with in-process parameters?	
	x	Does the section contain structural elucidation data?	
	x	Does the section contain specifications?	
	x	Does the section contain information on impurities?	
	x	Does the section contain validation data for analytical methods?	
	x	Does the section contain container and closure information?	
	x	Does the section contain stability data?	

2. Drug Product

x		Does the section contain manufacturing process with in-process controls?	
x		Does the section contain quality controls of excipients?	
x		Does the section contain information on composition?	
x		Does the section contain specifications?	
x		Does the section contain information on degradation products?	
x		Does the section contain validation data for analytical methods?	
x		Does the section contain information on container and closure systems?	
x		Does the section contain stability data with a proposed expiration date?	
x		Does the section contain information on labels of container and cartons?	
x		Does the section contain tradename and established name?	

C. Review Issues

x		Has all information requested during the IND phases, and at the pre-NDA meetings been included?	
	x	Is a team review recommended?	

x		Are DMFs adequately referenced?	

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On Original

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/s/

Shulin Ding
8/27/2008 01:07:59 PM
CHEMIST

Moo-Jhong Rhee
8/27/2008 01:11:12 PM
CHEMIST
Chief, Branch III

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Application:	NDA 22327/000	Action Goal:	
Stamp:	16-JUL-2008	District Goal:	17-MAR-2009
Regulatory Due:	16-MAY-2009	Brand Name:	LANSOPRAZOLE
Applicant:	NOVARTIS CONS	Estab. Name:	
	1400 SOUTH ORANGE AVE	Generic Name:	LANSOPRAZOLE
	ORLANDO, FL 32806		
Priority:	5S	Dosage Form:	(DELAYED RELEASE CAPSULE
Org Code:	560	Strength:	15 MG

Application Comment:

FDA Contacts:	S. GOLDIE	301-796-2055	, Project Manager
	M. YSERN	301-796-1487	, Review Chemist
	S. DING	301-796-1349	, Team Leader

Overall Recommendation: ACCEPTABLE on 12-MAY-2009by E. JOHNSON(HFD-320)301-796-3334

Establishment: CFN [redacted] FEI [redacted]

b(4)

b(4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE PACKAGER

Profile: CHG OAI Status: NONE

EMilestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	19-AUG-2008				DINGS
OC RECOMMENDATION	20-AUG-2008			ACCEPTABLE BASED ON PROFILE	KIEL

Establishment: CFN [redacted] FEI [redacted] b(4)

b(4)

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE RELEASE TESTER

Profile: CSN OAI Status: NONE

Estab. Comment: DRUG SUBSTANCE MANUFACTURE, TESTING AND RELEASE. (on 27-AUG-2008 by S.
DING () 301-796-1349)

Milestone Name	Date	Type	Insp. Date	Decision & Reason

Creator

SUBMITTED TO OC DINGS	27-AUG-2008			
♀ 19-MAY-2009 2 of 4	FDA CDER EES			Page

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

SUBMITTED TO DO ADAMSS	04-SEP-2008	GMP		
ASSIGNED INSPECTION T ADAMSS	12-NOV-2008	GMP		
INSPECTION PERFORMED JOHNSONE	27-APR-2009		27-APR-2009	
DO RECOMMENDATION JOHNSONE	29-APR-2009			ACCEPTABLE INSPECTION
OC RECOMMENDATION JOHNSONE	29-APR-2009			ACCEPTABLE DISTRICT RECOMMENDATION

Establishment: CFN 1911445 FEI 1911445

NOVARTIS CONSUMER HEALTH INC

10401 HWY 6

LINCOLN, NE 685179626

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE PACKAGER

FINISHED DOSAGE RELEASE TESTER

Profile: CHG OAI Status: NONE

Estab. Comment: THE SITE HAS FOUR FUNCTIONS: ENCAPSULATION/BANDING, DRUG PRODUCT
PACKAGING, DRUG PRODUCT RELEASE TESTING, AND DRUG PRODUCT STABILITY
TESTING.
PLEASE NOTE THAT THE FINISHED DOSAGE FORM IS A DELAYED RELEASE HARD
GELATINE CAPSULE. THIS SITE IS NOT INVOLVED IN THE MANUFACTURE OF THE
DELAYED RELEASE GRANULES, WHICH ARE MANUFACTURED ELSEWHERE AND SHIPPED
TO THIS SITE FOR ENCAPSULEATION/BANDING. (on 19-AUG-2008 by S. DING ()
301-796-1349)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	19-AUG-2008				DINGS
SUBMITTED TO DO	21-AUG-2008	GMP			FERGUSONS
ASSIGNED INSPECTION T	25-AUG-2008	GMP			SBERRYMA
INSPECTION PERFORMED	09-APR-2009		09-APR-2009		SBERRYMA
DO RECOMMENDATION	10-APR-2009			ACCEPTABLE	SBERRYMA

INSPECTION

A GMP/PAI WAS CONDUCTED 3/31-4/9/09 AND COVER THIS PRODUCT. A 2-ITEM FDA 483 WAS ISSUED
REGARDING RETAIN SAMPLES AND DOCUMENTATION OF TEMPERATURE MONITORING FOR THE RAW MATERIAL
WAREHOUSE. BASED ON INSPECTIONAL RESULTS, ——— RECOMMENDS APPROVABLE FOR THIS APPLICATION. b(4)

OC RECOMMENDATION 13-APR-2009 ACCEPTABLE
STOCKM

DISTRICT RECOMMENDATION

Establishment: CFN FEI ——— b(4)

b(4)

19-MAY-2009 FDA CDER EES Page
3 of 4

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE RELEASE TESTER

Profile: CHG OAI Status: NONE

Estab. Comment: THIS SITE INVOLVES ONLY ENCAPSUALTION/BANDING. IT IS NOT b(4)
INVOLVED IN THE MANUFACTURE OF DELAYED RELEASE GRANULES. (on
19-AUG-
2008 by S. DING () 301-796-1349)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	19-AUG-2008				DINGS
SUBMITTED TO DO	19-AUG-2008	10D			ADAMSS
DO RECOMMENDATION	29-AUG-2008			ACCEPTABLE	

ADAMSS

BASED ON FILE REVIEW

NAI GMP EI 5/2007

OC RECOMMENDATION 04-SEP-2008 ACCEPTABLE
ADAMSS

DISTRICT RECOMMENDATION

Establishment: CFN 9616691 FEI 3002870748

TAKEDA IRELAND LTD

BRAY BUSINESS PARK

KILRUDDERY, CO. WICKLOW, , EI

DMF No: AADA:

Responsibilities: INTERMEDIATE MANUFACTURER

INTERMEDIATE RELEASE TESTER

Profile: NEC OAI Status: NONE

Estab. Comment: THIS SITE MANUFACTURES DELAYED RELEASE GRANULATES, WHICH ARE SHIPPED TO

ELSEWHERE FOR ENCAPSUALTION/BANDING INTO HARD GELATINE CAPSULES. (on

27-AUG-2008 by S. DING () 301-796-1349)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	27-AUG-2008				DINGS
SUBMITTED TO DO	04-SEP-2008	GMP			ADAMSS
ASSIGNED INSPECTION T	12-NOV-2008	GMP			ADAMSS
INSPECTION SCHEDULED	07-MAY-2009		30-APR-2009		

IRIVERA

DO RECOMMENDATION JOHNSONE	12-MAY-2009	ACCEPTABLE
		INSPECTION
OC RECOMMENDATION JOHNSONE	12-MAY-2009	ACCEPTABLE
		DISTRICT RECOMMENDATION

Establishment: CFN 9610992 FEI 3002808311

TAKEDA PHARMACEUTICAL CO LTD

17-85 JUSO-HONMACHI 2-CHOME

YODOGAWA-KU, OSAKA, , JA 532-8686

DMF No: AADA:

ESTABLISHMENT EVALUATION REQUEST

DETAIL REPORT

Responsibilities: INTERMEDIATE MANUFACTURER

INTERMEDIATE RELEASE TESTER

Profile: CRU OAI Status: NONE

Estab. Comment: THE SITE MANUFACTURED DELAYED RELEASE GRANULES, WHICH ARE SHIPPED TO

ELSEWHERE TO BE ENCAPSULATED IN HARD GELATINE CAPSULES. (on 19-AUG-2008

by S. DING () 301-796-1349)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	19-AUG-2008				DINGS

SUBMITTED TO DO ADAMSS	19-AUG-2008	GMP	
DO RECOMMENDATION ADAMSS	16-JAN-2009		ACCEPTABLE BASED ON FILE REVIEW
OC RECOMMENDATION ADAMSS	16-JAN-2009		ACCEPTABLE DISTRICT RECOMMENDATION

Establishment: CFN 9610307 FEI 3002808306
TAKEDA PHARMACEUTICAL COMPANY LIMITED
4720 TAKEDA MITSUI
HIKARI, , JA

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE RELEASE TESTER

Profile: CSN OAI Status: NONE

Estab. Comment: DRUG SUBSTANCE MANUFACTURER, TESTING AND RELEASE (on 27-AUG-2008 by S.
DING () 301-796-1349)

Milestone Name	Date	Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	19-AUG-2008				DINGS
SUBMITTED TO DO	19-AUG-2008	GMP			ADAMSS
DO RECOMMENDATION	16-JAN-2009			ACCEPTABLE BASED ON FILE REVIEW	ADAMSS

OC RECOMMENDATION	16-JAN-2009	ACCEPTABLE
ADAMSS		
		DISTRICT RECOMMENDATION

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