CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 22410/S016

Trade Name: Suboxone® sublingual film

Generic Name: buprenorphine HCl & naloxone HCl dihydrate

Sponsor: Reckitt Benckiser Pharmaceuticals Inc.

Approval Date: 06/05/2014

Changes: addition of a new testing laboratory

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22410/S016

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22410/S016

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22410/S-016

APPROVAL LETTER

Reckitt Benckiser Pharmaceuticals Inc.
Attention: Bruce Paolella
Director Regulatory Strategy Category
10710 Midlothian Turnpike
Richmond VA 23235

Dear Mr. Paolella:

Please refer to your Supplemental New Drug Application (sNDA) dated and received December 6, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Suboxone (Buprenorphine HC1/ Naloxone HC1 Dihydrate) Sublingual Film.

This "Changes Being Effected in 30 Days" supplemental new drug application provides for addition of (b) (4) as an additional microbiological testing laboratory for the testing of raw material components and finished product

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call LCDR Luz E Rivera, Regulatory Project Manager, at (301) 796 4013.

Sincerely,

{See appended electronic signature page}

Ramesh Raghavachari, Ph.D.
Branch Chief, Branch IX,
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

RAMESH RAGHAVACHARI
06/05/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22410/S016

CHEMISTRY REVIEW(S)

Chemistry Review # 1	1. Division HFD-820	2. NDA Number ***22-410*** *Approved 8/30/2010*
3. Name and Address of Applicant *Reckitt Benckiser Pharmaceuticals Inc., 107010 Midlothian Turnpike, Richmond, VA 23235*		**4. Supplement** **Number** **Date** *S-16* *12/6/2013*
5. Name of Drug Suboxone (b) (4)	**6. Nonproprietary Name** *Buprenorphine/Naloxone (Schedule III)*	
7. CBE30 Supplement Provides for: *CTL, (b) (4), as an additional microbiological testing laboratory for testing raw material components and finished the drug product*		**8. Amendment(s)**
9. Pharmacological Category	**10. How Dispensed** Rx	**11. Related Documents**
12. Dosage Form *Film, Sublingual*	**13. Strength** *2mg/0.5mg, 4mg/1mg, 8mg/2mg, 12mg/3mg*	

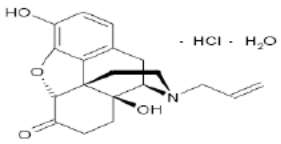
14. Chemical Name and Structure

Naloxone hydrochloride dihydrate

$C_{19}H_{21}NO_4 \cdot HCl \cdot 2H_2O$

MW: 399.9

CAS RN: 465-65-6 Naloxone.
357-08-4 Naloxone hydrochloride anhydrous
51481-60-8 Naloxone hydrochloride dihydrate



4,5α-Epoxy-3,14-dihydroxy-17-(prop-2-enyl)morphinan-6-one hydrochloride dihydrate

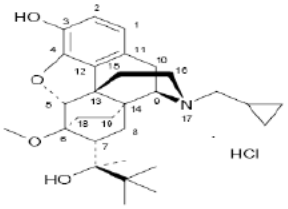
Buprenorphine hydrochloride

Laboratory Code: RX6029M.HCl

$C_{29}H_{41}NO_4 \cdot HCl$

MW: 467.6 (base) 504.1 (salt)

CAS Registry number: 53152-21-9



(2*S*)-2-[17-Cyclopropylmethyl-4,5α-epoxy-3-hydroxy-6-methoxy-6α,14-ethano-14α-morphinan-7α-yl]-3,3-dimethylbutan-2-ol hydrochloride

15. Comments: *EES is acceptable for CTL to recommend an approval action for NDA 22410/S-17. Enclosed is EES report. The sponsor certifies that (b) (4) is capable of performing microbiological testing in accordance with USP 61 and 62, and module 3.2.P.3.1 was updated.* (b) (4) *claims in a letter dated 10/15/2013 that cGMP quality systems are in place.* (b) (4) *claims in a letter dated 9/30/2013 that the site is a registered facility with DEA and FDA to provide microbiological testing services.* (b) (4) (b) (4) *Monosol Rx is a contractor to the sponsor to manufacture the drug product at* (b) (4) *facilities in* (b) (4).

16. Conclusions and Recommendations

NDA 22-410/S-14 is recommended for an approval action.

17. Name	**Signature**	**Date**
Dr. Pramoda Maturu, Ph.D, Senior Regulatory Review Chemist		
Dr. Ramesh Raghavachari, PhD, Branch Chief		

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 22410/016

Stamp Date: 06-DEC-2013

Regulatory: 06-JUN-2014

Action Goal:

District Goal: 02-MAY-2014

Applicant: RECKITT BENCKISER
10710 MIDLOTHIAN TPKE STE 430
RICHMOND, VA 23235

Brand Name: SUBOXONE (BUPRENORPHINE/NALOXONE) SUBLIN

Estab. Name:

Generic Name:

Priority: 4S

Org. Code: 170

Product Number; Dosage Form; Ingredient; Strengths

001; FILM; NALOXONE HYDROCHLORIDE; EQ .5MG BASE
001; FILM; BUPRENORPHINE HYDROCHLORIDE; EQ 2MG BASE
002; FILM; BUPRENORPHINE HYDROCHLORIDE; EQ 8MG BASE
002; FILM; NALOXONE HYDROCHLORIDE; EQ 2MG BASE
003; FILM; NALOXONE HYDROCHLORIDE; EQ 1MG BASE
003; FILM; BUPRENORPHINE HYDROCHLORIDE; EQ 4MG BASE
004; FILM; NALOXONE HYDROCHLORIDE; EQ 3MG BASE
004; FILM; BUPRENORPHINE HYDROCHLORIDE; EQ 12MG BASE

Application Comment:

FDA Contacts:	P. MATURU	Prod Qual Reviewer		3017961707
	L. RIVERA	Product Quality PM		3017964013
	M. SULLIVAN	Regulatory Project Mgr	(HFD-170)	3017961245
	M. GAUTAM BASAK	Team Leader	(HFD-510)	3017960712

Overall Recommendation:	ACCEPTABLE	on 25-APR-2014	by T. SHARP	()	3017963208
	PENDING	on 08-JAN-2014	by EES_PROD		

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)

DMF No: AADA:

Responsibilities: FINISHED DOSAGE OTHER TESTER

Establishment Comment: MICROBIOLOGICAL TESTING OF RAW MATERIALS & FINISHED DRUG PRODUCT (on 08-JAN-2014 by L. RIVERA () 3017964013)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

Milestone Name	Milestone Date	Request Type	Planned Completion	Decision	Creator
Comment					
OAI Submit To OC					
Request to Extend Re-eval Date To					
Extension Request Comment					
Reason					
SUBMITTED TO OC	08-JAN-2014				RIVERAL
SUBMITTED TO DO	09-JAN-2014	Product Specific and GMP Inspection			WILSONT
1ST FDA EVLA. PDUFA 02-MAY-2014					
ASSIGNED INSPECTION TO IB	16-JAN-2014	Product Specific and GMP Inspection			(b) (4)
FIRST FDA EVALUATION - PDUFA MAY 2014 (MAY 2ND)					

INSPECTION PERFORMED (b) (4) (b) (4) (b) (4)

This was a directed NDA pre-approval inspection of a contracted testing laboratory that performs testing for a client relevant to their NDA #22410 (supplement 16), under which (b) (4) (hereafter (b) (4), the lab, this facility, or the firm) is listed as Finished Dosage other tester. This inspection focused on (b) (4) testing capacity, specifically, what kind of drug substance testing the firm performs, and what they are capable of performing; their good manufacturing practices (cGMPs), and was conducted under Compliance Program 7356.002 Drug Manufacturing Inspections, as well as 7346.832 Pre-Approval Inspections / Investigations.

This was the first inspection performed at this facility. The firm is a stand-alone business that was established and incorporated in the state of (b) (4) on (b) (4) and operated as a (b) (4) firm until (b) (4) when it purchased this facility, providing space to perform contracted laboratory testing and production of (b) (4) They expect to have a (b) (4) (b) (4) by (b) (4).

The current inspection focused on the Quality, Equipment, and Laboratory systems, especially the firm's validation of their microbial limit testing procedures, and the incubators used to perform these tests (b) (4) (b) (4) (b) (4) Applicant Reckitt Benckiser, located at 1070 Midlothian Turnpike Suite 43, Richmond, VA 23235. No deficiencies were noted.

A review of the FACTS Consumer Complaints database found no complaints have been filed against the firm since January 01, 2001. (b) (4) stated they had received one complaint about their (b) (4) one customer found the (b) (4) The root cause discovered was that their (b) (4) (b) (4) had not verified the (b) (4) applied to the (b) (4) the problem has not appears this way on original

DO RECOMMENDATION PRE APPROVAL EI/GMP INSPECTION DATED (b) (4) FOUND NAI WITH RECOMMENDATION FOR APPROVAL.	21-APR-2014		ACCEPTABLE	(b) (4)
OC RECOMMENDATION 3YR FOR CTL	25-APR-2014		ACCEPTABLE	SHARPT

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/s/

PRAMODA K MATURU
06/04/2014

RAMESH RAGHAVACHARI
06/04/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22410/S016

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 22410/S-016

CBE-30 SUPPLEMENT ACKNOWLEDGEMENT

Reckitt Benckiser Pharmaceuticals Inc.
Attention: Bruce Paolella
Director Regulatory Strategy Category
10710 Midlothian Turnpike
Richmond VA 23235

Dear Mr. Paolella:

We have received your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA NUMBER: 22410

SUPPLEMENT NUMBER: 016

PRODUCT NAME: Suboxone (Buprenorphine HC1/ Naloxone HC1 Dihydrate) Sublingual Film

DATE OF SUBMISSION: December 6, 2013

DATE OF RECEIPT: December 6, 2013

This supplemental application, submitted as a "Changes Being Effected in 30 Days" supplement, proposes to add [redacted] (b) (4) as an additional microbiological testing laboratory for the testing of raw material components and finished product.

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 4, 2014, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be June 6, 2014.

Cite the application 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 Anesthesia, Analgesia and Addiction Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have questions, call me, at (301) 796- 4013

Sincerely,

LCDR Luz E Rivera, Psy.D.
Regulatory Project Manager
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

LUZ E RIVERA
01/08/2014