

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-717/S-004

Name: Provigil Tablets

Generic Name: modafinil

Sponsor: Cephalon, Inc.

Approval Date: 11/05/01

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**APPLICATION NUMBER:
NDA 20-717/S-004**

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APPLICATION NUMBER:

NDA 20-717/S-004

APPROVAL LETTER



NDA 20-717/S-004

Cephalon, Inc.
Attention: Kenneth L. White, PharmD.
Vice President, Regulatory Affairs
145 Brandywine Parkway
West Chester
PA 19380-4245

Dear Mr. White:

Please refer to your supplemental new drug application dated July 13, 2001, received July 16, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Provigil (modafinil) Tablets, 100 mg and 200 mg.

This supplemental new drug application provides for the addition of an alternate manufacturing site, Catalytica, NC, for the manufacture of Provigil Tablets.

We acknowledge receipt of your submission dated October 25, 2001.

We have completed the review of this supplemental application as amended, and it 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 Anna Marie Homonnay, R.Ph., Regulatory Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Maryla Guzewska, Ph.D.
Chemistry Team Leader, Neurology Drugs for the
Division of Neuropharmacological Drug Products,
(HFD-120)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Maryla Guzewska
11/5/01 02:56:00 PM

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APPLICATION NUMBER:

NDA 20-717/S-004

CHEMISTRY REVIEW(S)

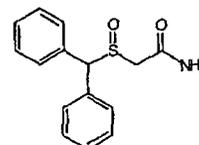
**CHEMIST'S REVIEW
OF SUPPLEMENT**

ORGANIZATION: HFD-120
NDA NUMBER: 20-717
SUPPLEMENT NUMBER: SCM-004

LETTER DATE 13-JUL-01
STAMP DATE 16-JUL-01
AMENDMENTS:
LETTER DATES 25-OCT-01
STAMP DATES 26-OCT-09

RECEIVED BY CHEMIST: 18-JUL-01

APPLICANT NAME AND ADDRESS: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245
NAME OF DRUG: Provigil®
NONPROPRIETARY NAME: Modafinil
CHEMICAL NAME / STRUCTURE: 2-[(Diphenylmethyl)sulfinyl]acetamide



DOSAGE FORM(S): Tablets
POTENCY(IES): 100 mg, 200 mg
PHARMACOLOGICAL CATEGORY: Narcolepsy
SPECIAL PRODUCTS: (YES) XX (NO)
HOW DISPENSED: XX (Rx) (OTC)
RECORDS / REPORTS CURRENT: XX (YES) (NO)
RELATED IND / NDA / DMF(S):

SUPPLEMENT PROVIDES FOR: The addition of an alternate manufacturing site, Catalytica, NC, for the drug product.

COMMENTS: This is a PA supplement for a SUPAC L3 change. The sponsor describes minor changes in the manufacturing and packaging as a result of the site transfer. The supplement contains batch records of the validation batches from the new site as well as their release batch results. The amendment dated October 25 provides comparative multi-point dissolution data to support the site transfer. These data were reviewed by the Biopharmaceuticals Division. The dissolution profiles at the two manufacturing sites were concluded to be similar (see Biopharm. Review dated October 31, 2001). Available stability results are also provided. All six batches meet the same specifications as approved in the NDA. The testing methods remain the same and have undergone technology transfer. Labeling is adjusted to reflect the additional site and new identification numbers. The site was inspected and received an Acceptable recommendation from the Office of Compliance (see EER in CMC Review Notes).

CONCLUSIONS AND RECOMMENDATIONS: Recommend Approval based on OC and Biopharmaceutical Division recommendations.

<u>REVIEWER NAME</u>	<u>SIGNATURE</u>	<u>DATE COMPLETED</u>
Mona Zarifa, Ph.D.		November 5, 2001

cc: Orig: NDA 20-717
HFD-120/Div. File
HFD-120/Ahomonnay/Mzarifa/MGuzewska

INIT: MGuzewska

Filename: 20717s4.doc

Redacted 6 page(s)

of trade secret and/or

confidential commercial

information from

S-004. Chemistry Review

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/s/

Mona Zarifa
11/5/01 02:45:36 PM
CHEMIST

Maryla Guzewska
11/5/01 02:50:01 PM
CHEMIST

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APPLICATION NUMBER:

NDA 20-717/S-004

**CLINICAL PHARMACOLOGY/
BIOPHARMACEUTICS REVIEW(S)**

OFFICE OF CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW

Submission Date: 7/13/01, 10/25/01

NDA: 20-717/SCM-004
Drug Name: Provigil® (modafinil) 100mg and 200mg Tablets
Indication: Narcolepsy
Sponsor: Cephalon Inc. West Chester PA
Type of Document: CMC Site Change Supplement
Reviewer: Hong Zhao, Ph.D.

Introduction

The purpose of this Supplement is to provide data to support the addition of DSM Catalytica Pharmaceuticals, Inc., Greenville, NC (Catalytica) as an alternate site to manufacture, package and perform analytical testing of PROVIGIL drug product (100 and 200 mg) Tablets for commercial use.

Dissolution Data Review

Multipoint dissolution profile data were generated using the NDA approved dissolution method (USP Dissolution Apparatus II, a paddle speed of 50 rpm and 900 mL 0.1 N HCl dissolution medium):

Mean % Dissolved ±SD

Time (min)	□ (N=12) (100 mg Tablet)		Catalytica (N*=18)	
	1538-FL5	1538-FL15	9K6019	9L6002
15	80±10.2	82±9.8	79±5.4	77±8.0
30	94±6.3	93±7.8	95±2.3	93±5.2
45	97±4.9	99±5.6	98±2.0	95±4.4
60	99±4.2	100±5.2	98±1.8	96±4.1

Time (min)	□ (N=6) (200 mg Tablet)		Catalytica (N*=18)			
	1538-FL2	1538-FL4	1538-FL6	1538-FL8	050960	9K6020
15	88±3.5	79±3.6	79±4.5	76±2.9	77±6.7	73±8.2
30	97±1.2	93±1.6	95±1.5	91±1.2	92±3.4	91±2.7
45	98±0.6	96±1.1	98±0.9	95±0.9	97±2.7	95±1.6
60	98±0.6	96±1.2	98±0.8	96±0.8	#	96±1.3

N*=18 values derived from 6 beginning + 6 middle + 6 end samples. # Sampling stopped at 45 minutes.

Lot Summary

Lot #	Strength	Manufacturer	Description
1538-FL5	100 mg	□	NDA Regis. @ □
1538-FL15	100 mg	□	NDA Regis. @ □
9L6002	100 mg	Catalytica	Pilot lot
9K6019	100 mg	Catalytica	Pilot lot
1538-FL2	200 mg	□	NDA Regis. @ □
1538-FL4	200 mg	□	NDA Regis. @ □
1538-FL6	200 mg	□	NDA Regis. @ □
1538-FL8	200 mg	□	NDA Regis. @ □
050960	200 mg	□	Recent Commercial lot
9K6020	200 mg	Catalytica	Pilot lot

Summary

- The regulatory dissolution specification for PROVIGIL Tablets is NLT 90% in 45 minutes.
- The dissolution performance for all lots tested meet the regulatory specification for PROVIGIL Tablets.
- PROVIGIL Tablets manufactured at [] site and the proposed site (Catalytica) dissolved rapidly with >90% of the drug dissolved in 30 minutes for all the lots tested.

Comment 1

PROVIGIL Tablets 100 and 200 mg manufactured at the proposed site (Catalytica) have similar dissolution profiles as compared to that of the drug products manufactured at the approved site [] .

Recommendation

Please convey Comment 1 to Chemistry Review team.

Hong Zhao, Ph.D. _____

RD/FT Initialed by Raman Baweja, Ph.D. _____

cc: NDA 20-717 (CMC Site Change Supplement), HFD-120, HFD-860 (Zhao, Baweja, Mehta), Central Documents Room (CDR-Biopharm)

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/s/

Hong Zhao
10/31/01 03:25:57 PM
BIOPHARMACEUTICS

Raman Baweja
10/31/01 04:14:45 PM
BIOPHARMACEUTICS

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APPLICATION NUMBER:

NDA 20-717/S-004

ADMINISTRATIVE and
CORRESPONDENCE DOCUMENTS



NDA 20-717

PRIOR APPROVAL SUPPLEMENT

Cephalon, Inc.
Attention: Paul M. Kirsch
Director, U.S. Regulatory Operations
145 Brandywine Parkway
West Chester, PA 19380-4245

Dear Mr. Kirsch,

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

Name of Drug Product:	PROVIGIL (modafinil) Tablets
NDA Number:	20-717
Supplement number:	S-004
Date of supplement:	July 13, 2001
Date of receipt:	July 16, 2001

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 16, 2001 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Neuropharmacological Drug Products, HFD-120
Attention: Division Document Room, 4008
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Neuropharmacological Drug products, HFD-120
Attention: Division Document Room, 4008
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, call Anna Marie Homonnay, R.Ph., Regulatory Management Officer, at (301) 594-2850.

Sincerely,

{See appended electronic signature page}

Maryla Guzewska, Ph.D.
Chemistry Team Leader, Neurology Drugs for the
Division of Neuropharmacological Drug Products
(HFD-120)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Maryla Guzewska
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