

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020717

CHEMISTRY REVIEW(S)

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 20-717

CHEMISTRY REVIEW: # 1

DATE REVIEWED: 21-APR-97

Submission Type
ORIGINAL

Document Date
27-DEC-96

CDER Date
30-DEC-96

Assigned Date
07-JAN-97

NAME AND ADDRESS OF APPLICANT: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245

DRUG PRODUCT NAME:

Proprietary: PROVIGIL
Nonproprietary/Established/USAN: modafinil
Code Name/#: CEP-1538
Chem. Type/Ther. Class: 1 S

DESI/PATENT STATUS: Modafinil has Orphan Drug status

PHARMACOLOGICAL CATEGORY/INDICATION: Narcolepsy

DOSAGE FORM: Tablets

STRENGTH(S): 100 mg, 200 mg

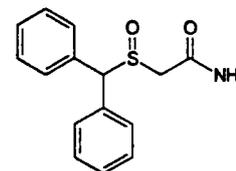
ROUTE OF ADMINISTRATION: Oral

DISPENSED: XX Rx ___ OTC

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:

2-[(Diphenylmethyl)sulfinyl]acetamide, CAS No. 68693-11-8

C₁₅H₁₅NO₂S Mol. Weight: 273.34



SUPPORTING DOCUMENTS: DMF [REDACTED], DMF [REDACTED]
[REDACTED] and DMF [REDACTED]

RELATED DOCUMENTS (if applicable): IND [REDACTED]

CONSULTS: Environmental Assessment - Consulted to HFD-357 by Project Manager, not complete

REMARKS/ COMMENTS:

[REDACTED] Cephalon will not be doing any of the actual manufacturing and release testing of the product. Drug substance will be manufactured in [REDACTED] by a [REDACTED] subsidiary [REDACTED] and Modafinil tablets will be manufactured in the [REDACTED] [REDACTED] DMF [REDACTED] covering [REDACTED] has been reviewed [REDACTED] Inspections and EA review and method validation are not done. Ther are some deficiencies in the NDA itself [REDACTED] these are relatively minor.

CONCLUSIONS AND RECOMMENDATIONS:

Recommend Information Request letter to sponsor.

cc: Orig. NDA 20-717
HFD-120/Division File
HFD-120/MHeimann/21-APR-97
HFD-120/SHardeman /S/
HFD-120/SBlum/Init. [REDACTED]

[REDACTED] 4/21/97
Martha R. Heimann, Ph.D., Review Chemist
Filename: N20-717.001

4/21/97
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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 20-717

CHEMISTRY REVIEW: #2

DATE REVIEWED: 02-DEC-97

Submission Type	Document Date	CDER Date	Assigned Date
N(BC), revised Env. Ass.	02-MAY-97	05-MAY-97	05-MAY-97
N(BC), responses to IR letter	28-JUL-97	29-JUL-97	29-JUL-97
N(BC), responses to IR letter	02-SEP-97	03-SEP-97	03-SEP-97
N(BZ)	22-SEP-97	23-SEP-97	23-SEP-97

NAME AND ADDRESS OF APPLICANT: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245

DRUG PRODUCT NAME:

Proprietary: PROVIGIL
Nonproprietary / Established / USAN: modafinil [adopted 1994]
Code Name / #: CEP-1538
Chem. Type / Ther. Class: 1 S

DESI / PATENT STATUS: Modafinil drug substance, and the drug product formulation, are licensed to Cephalon by the French developer, Laboratoire Lafon.

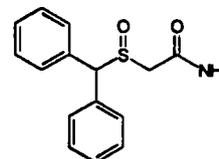
PHARMACOLOGICAL CATEGORY / INDICATION: Narcolepsy (Orphan Drug status)

DOSAGE FORM: Tablets
STRENGTH(S): 100 mg, 200 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:

2-[(Diphenylmethyl)sulfinyl]acetamide, CAS No. 68693-11-8

C₁₅H₁₅NO₂S Mol. Weight: 273.36



SUPPORTING DOCUMENTS: DMF [redacted] and DMF [redacted]

RELATED DOCUMENTS (if applicable): IND [redacted]

CONSULTS: Environmental Assessment - Consulted to HFD-357, FONSI issued 25-JUN-97

REMARKS / COMMENTS:

The sponsor has addressed all concerns from the 12-MAY-97 Information request letter but the 'alternative'

CONCLUSIONS AND RECOMMENDATIONS:

Recommend Approvable for Chemistry pending resolution of foreign inspection. Action letter should contain standard paragraph concerning completion of methods validation. [redacted]

cc: Orig. NDA 20-717
HFD-120/Division File
HFD-120/MHeimann/02-DEC-97
HFD-120/MMalandrucco
HFD-120/MGuzewska/Int. [redacted]

2.297

12/2/97
Martha R. Heimann, Ph.D., Review Chemist
Filename: N20-717.002

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA#: 20-717

CHEMISTRY REVIEW: # 3

DATE REVIEWED: 16-JUL-98

Submission Type	Document Date	CDER Date	Assigned Date
N(BZ) partial response to AE letter	30-MAR-98	31-MAR-98	31-MAR-98
NC	06-MAY-98	07-MAY-98	07-MAY-98

NAME AND ADDRESS OF APPLICANT: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245

DRUG PRODUCT NAME:

Proprietary: PROVIGIL
Nonproprietary/Established/USAN: modafinil [adopted 1994]
Code Name/#: CEP-1538
Chem. Type/Ther. Class: 1 S

DESI/PATENT STATUS: Modafinil drug substance, and the drug product formulation, are licensed to Cephalon by the French developer, Laboratoire Lafon.

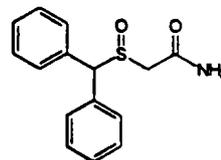
PHARMACOLOGICAL CATEGORY/INDICATION: Narcolepsy (Orphan Drug status)

DOSAGE FORM: Tablets
STRENGTH(S): 100 mg, 200 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA AND MOLECULAR FORMULA:

2-[(Diphenylmethyl)sulfinyl]acetamide, CAS No. 68693-11-8

C₁₅H₁₅NO₂S Mol. Weight: 273.36



SUPPORTING DOCUMENTS: DMF [redacted] DMF [redacted]
[redacted] and DMF [redacted]

RELATED DOCUMENTS (if applicable): IND [redacted]

CONSULTS: Environmental Assessment - Consulted to HFD-357, FONSI issued 25-JUN-97

REMARKS/COMMENTS:

[redacted]

The sponsor submitted two amendments in response to the 29-DEC-97 approvable letter. The first submission (30-MAR-98) contains adequate responses to the two remaining CMC related review issues; i.e., the expiration dating period requested by the sponsor and the adoption of uniform dissolution specifications for both tablet strengths. The 30-MAR-98 amendment provides real time data to support the proposed 3 year expiry. The 06-MAY-98 submission is a request for Agency concurrence with a stability matrix plan to be used to support post-approval changes [redacted]

CONCLUSIONS AND RECOMMENDATIONS:

Recommend Approval for Chemistry. Action letter should contain standard paragraph concerning completion of methods validation. [redacted]

cc: Orig. NDA 20-717
HFD-120/Division File
HFD-120/MHeimann/16-JUL-98
HFD-120/AHommonay
HFD-120/MGuzewska/Init [redacted] 17.98

/S/ [redacted] 7/16/98
Martha R. Heimann, Ph.D., Review Chemist
Filename: N20-717.003

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020717

ENVIRONMENTAL ASSESSMENT AND/OR FONSI

ENVIRONMENTAL ASSESSMENT
AND
FINDING OF NO SIGNIFICANT IMPACT
FOR

Provigil®
(Modafinil)
Tablet
NDA 20-717

Cephalon® Inc.

U. S. FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Division of Neuropharmacological Drug Products
(HFD-120)

FINDING OF NO SIGNIFICANT IMPACT

NDA 20-717

Provigil®

(Modafinil)

Tablets

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions. FDA is required under NEPA to consider the environmental impact of approving certain drug product applications as an integral part of its regulatory process.

The Food and Drug Administration, Center for Drug Evaluation and Research, has carefully considered the potential environmental impact of this action and has concluded that it will not have a significant effect on the quality of the human environment and that an environmental impact statement therefore will not be prepared.

In support of their new drug application for Provigil®, Cephalon® Inc., prepared an environmental assessment (attached) in accordance with 21 CFR 25.31a(b)(3), which evaluates the potential environmental impact of the manufacture, use and disposal of the product.

Modafinil is a [REDACTED] drug which is administered as a tablet to increase wakefulness in patients with excessive daytime sleepiness associated with narcolepsy. The drug product will be manufactured by Circa Pharmaceuticals, Copiague, New York. The finished drug product will be used by patients in hospitals, clinics and in their homes.

Modafinil may enter the environment from excretion by patients, from disposal of pharmaceutical waste or from emissions from manufacturing sites.

Disposal of the drug may result from out of specification lots, discarding of unused or expired product, and user disposal of empty or partly used product and packaging. Returned drug product will be disposed of at a licensed incineration or landfill facility. At U.S. hospitals and clinics, empty or partially empty packages will be disposed according to hospital/clinic regulations. From home use, empty or partially empty containers will typically be disposed of by a community's solid waste management system which may include landfills, incineration and recycling, while minimal quantities of unused drug may be disposed of in the sewer system.

The Center for Drug Evaluation and Research has concluded that the product can be manufactured, used and disposed of without any expected adverse environmental effects. Precautions taken at the sites of manufacture of the bulk product and its final formulation are expected to minimize occupational exposures and environmental release. Adverse effects are not anticipated upon endangered or threatened species or upon property listed in or eligible for listing in the National Register of Historic Places.

/s/

PREPARED BY
Carl J. Berninger, Ph.D.
Environmental Scientist
Environmental Assessment Team
Center for Drug Evaluation and Research

6/24/97
Date

/s/

CONCURRED
Nancy B. Sager
Team Leader
Environmental Assessment Team
Center for Drug Evaluation and Research

6/25/97
Date

Attachments: Environmental Assessment (FOI copy)
Material Safety Data Sheet for drug substance

APPEARS THIS WAY ON ORIGINAL

FONSI for NDA 20-717

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ENVIRONMENTAL ASSESSMENT

NON-CONFIDENTIAL

NDA 20-717

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Environmental Assessment for Modafinil Tablets

ITEM 1. Date:

April 30, 1997
(Supercedes October 11, 1996)

ITEM 2. Name of Applicant:

Cephalon[®], Inc.

ITEM 3. Address:

145 Brandywine Parkway
Building 300
West Chester, PA 19380-4245

ITEM 4. Description of Proposed Action:

A. Requested Approval:

FDA approval for the manufacture and commercial distribution of modafinil tablets in the United States. Approval is being sought for a NDA for a human drug intended for the treatment of patients with a rare disease (*i.e.*, treatment to increase wakefulness in patients with excessive daytime sleepiness associated with narcolepsy). Modafinil was designated as an orphan drug product for treatment of this indication on March 15, 1993. As a result, this environmental assessment has been prepared using the abbreviated format provided in 21 CFR §25.31a(b)(3).

B. Need for the Action (Proposed Use):

Modafinil is indicated to increase wakefulness in patients with excessive daytime sleepiness associated with narcolepsy.

C. Description of Drug Product

Information on the composition and components of modafinil tablets is presented in confidential Appendix A. The drug product will be available in tablet formulations containing either 100 mg or 200 mg of modafinil. [REDACTED]

D. Production Locations:

1. Manufacturing of the key intermediate used in modafinil synthesis:

The key intermediate used in modafinil synthesis will be produced by a foreign contract manufacturer. The identity of this intermediate and the contractor are considered proprietary and are given in confidential Appendix B. The contractor's manufacturing site is approximately [REDACTED] in size, located in a temperate region near a large metropolitan area. The site is in an industrial area surrounded by a mix of industry and warehouses and located adjacent to large river. The nearest residential area is across the river from the site. See confidential Appendix B for additional information.

2. Manufacturing of the drug substance (modafinil):

The drug substance will be produced by a foreign contract manufacturer. The identity of this contractor is considered proprietary and is given in confidential Appendix C. The contractor's production site is [REDACTED] in size, located near a large metropolitan area in a temperate region. The plant is about 3 km west of a small village, surrounded by a mix of light industrial and commercial development. The facility is situated on flat land approximately 15 km from a river. See confidential Appendix C for additional information.

3. Manufacture and packaging of the drug product (modafinil tablets):

The drug product will be contract manufactured and packaged at [REDACTED]. A certification of compliance by Circa Pharmaceuticals is provided in Appendix D. The manufacturing site is located in a temperate region on flat land. The site is approximately [REDACTED] in size, surrounded by a mix of industrial, commercial and residential development. There are no significant water bodies (rivers, lakes, or oceans) within 1.6 km of the facility. See confidential Appendix E for additional information.

E. Locations of Use:

Modafinil tablets will be distributed by, or on behalf of, Cephalon®, Inc. to hospitals and pharmacies throughout the U.S. for prescription use by patients with narcolepsy.

F. Disposal Sites

Cephalon®, Inc. will request that all unsold or expired modafinil tablets be returned to a contract facility in the United States for disposal. Returned, expired, or rejected drug product will be disposed of at a facility which is licensed by the EPA or an appropriate state authority to destroy hazardous materials. The identity of this contractor is considered proprietary and is given in confidential Appendix F.

ITEM 5. Identification of Chemical Substances that are the Subject of the Proposed Action:

The active drug substance in modafinil tablets is modafinil. Table 1 summarizes information on the identity of this substance. The structure of modafinil is depicted in Figure 1.

Table 1: Identification of Drug Substance in Modafinil Tablets	
Parameter	Description
Common Use Name	modafinil
Chemical Names	2-[(diphenylmethyl)sulfinyl]acetamide 2-(benzhydrylsulfinyl)acetamide
CAS Reg. No.	68693-11-8
Molecular weight	273.36
Molecular formula	$C_{15}H_{15}NO_2S$
Physical description	White to off-white crystalline powder
Expected impurities	modafinil acid $\leq 0.5\%$ (2-[(diphenylmethyl)sulfinyl]acetic acid) modafinil sulfone $\leq 0.5\%$ (2-[(diphenylmethyl)sulfonyl]acetamide) modafinil ester $\leq 0.5\%$ (methyl 2-[(diphenylmethyl)sulfinyl]acetate) Unknowns $\leq 0.1\%$ Total $\leq 1.5\%$
Expected degradation products	modafinil acid (2-[(diphenylmethyl)sulfinyl]acetic acid) modafinil sulfone (2-[(diphenylmethyl)sulfonyl]acetamide)

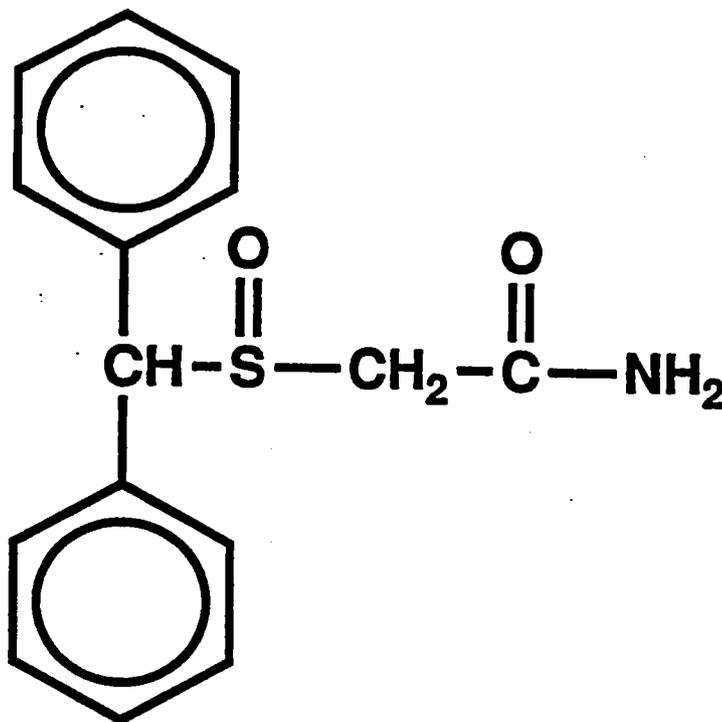


FIGURE 1. Structure of Modafinil

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Modafinil is a white to off-white crystalline powder with a molecular weight of 273.36. It is practically insoluble in water and cyclohexane. It is sparingly to slightly soluble in methanol and acetone (NDA #20,717; Item 3; Chemistry, Manufacturing and Control Section). A material safety data sheet (MSDS) for modafinil drug substance is provided in Appendix G.

ITEM 6. Introduction of Substances into the Environment:

A. Contract Manufacturing Facility - Key Intermediate

The key intermediate used in the synthesis of modafinil will be produced at a foreign contract facility. Because this is a foreign facility with appropriate certification (see below), no information is being provided regarding substances to be emitted or controls exercised. This facility is currently in compliance with all applicable environmental laws and emission requirements. A certified statement of compliance for this facility is contained in confidential Appendix B. Approval of the proposed action is expected to have no effect on compliance with current emission requirements at this facility.

B. Contract Manufacturing Facility - Drug Substance (Modafinil)

The drug substance modafinil will be manufactured at a foreign contract facility. Because this is a foreign facility with appropriate certification (see below), no information is being provided regarding substances to be emitted or controls exercised. This facility is currently in compliance with applicable environmental laws and emission requirements. A certified statement of compliance for this facility is contained in confidential Appendix C. Approval of the proposed action is expected to have no effect on compliance with current emission requirements at this facility.

C. Manufacture and Packaging of Drug Product - Modafinil Tablets:

██████████, a contract facility located in ██████████ will formulate and package the drug product for Cephalon[®], Inc. This contract facility is an existing facility that currently manufactures solid dosage forms and gum products for itself and other companies. The facility operates under Good Manufacturing Practices and is registered with the FDA. The Drug Establishment Registration number for the facility is given in confidential Appendix E.

1. Substances Expected to be Emitted

Appropriate controls are exercised to limit potential emissions to air and wastewater and to limit occupational exposures to the drug substance and excipients. Because of the in-place emission controls, neither modafinil nor any of the other drug product or packaging components, or process aids are expected to be released to air or water in sufficient quantities to produce any significant environmental impact (see confidential Appendix E).

2. Controls Exercised

Air Handling and Treatment: All manufacturing and packaging areas are connected to a non-recirculating dust collection system. The system removes particles by vacuum action, controlling the amount of dust in manufacturing areas.

Wastewater Handling and Treatment: All manufacturing and packaging buildings are connected to the local municipal sewage collection system. All treatment of wastewater is performed at the local municipal wastewater treatment plant. A spill prevention plan is in place and responses are governed by a company Standard Operating Procedure (SOP). Depending on the type of spill (hazardous or non-hazardous), one of two waste disposal companies is asked to respond (see confidential Appendix E).

Disposal of Production Waste and Non-Usable Product: All significant production waste and non-usable product is collected for destruction by incineration by licensed disposal companies. This includes laboratory solvents, acids, and bases. Information on the companies used for disposal of hazardous and non-hazardous waste, including permit numbers, is presented in confidential Appendix E.

Occupational Exposure: Appropriate safety precautions are observed during all manufacturing operations to prevent occupational exposures. Employees are given instructions regarding safe product handling procedures and are provided with proper safety clothing and protective equipment (*i.e.*, masks, gloves, uniforms, etc.). Respirators are used during the manufacture of modafinil tablets. These respirators are OSHA recommended, with filters appropriate for handling various solvents and acid/base materials. Material Safety Data Sheets (MSDSs) are obtained and retained in the company files for each material handled at the facility. MSDSs are readily available and accessible to employees for their reference.

3. Citation of, and Statement of Compliance with, Applicable Emission Requirements

Circa Pharmaceuticals holds several "Permits to Operate" for air emissions from the appropriate state regulatory agency. A listing of these permits, including permit numbers, expiration dates, and authorized activities, is presented in confidential Appendix E.

For wastewater handling and treatment, Circa Pharmaceuticals has a discharge certification, but not a specific discharge permit, from the local municipal sewer district. Sewer district authorities monitor the effluent that leaves each building and have determined that the facility discharges do not exceed the relevant limits for pH, color, total suspended solids (TSS), and biochemical oxygen demand (BOD).

In addition to these permits and certifications, Circa Pharmaceuticals has U.S. Environmental Protection Agency "Acknowledgment of Notification of Hazardous Waste Activity" and necessary identification numbers (see confidential Appendix E).

Circa Pharmaceuticals operates in compliance with all emission requirements, including occupational, set forth in applicable federal, state and local environmental laws, regulations, and permits. A certified statement of compliance for this facility is included in Appendix D.

4. Effect of Approval on Compliance with Applicable Emission Requirements

Circa Pharmaceuticals currently manufactures formulated drug products for itself and other companies. Approval of the proposed action and subsequent manufacture of production quantities of modafinil tablets will not significantly increase facility production and, therefore, is not expected to affect facility compliance with current discharge or emission requirements.

D. Estimate of Maximum Yearly Market Volume:

An estimate of the maximum yearly market volume for modafinil tablets is contained in confidential Appendix H.

ITEMS 7-11. Fate of Emitted Substances in the Environment; Environmental Effects of Released Substances; Use of Resources and Energy; Mitigation Measures; and Alternatives to the Proposed Action:

Approval is being sought for a NDA for a human drug intended for the treatment of patients with a rare disease. Modafinil was designated as an orphan drug product on March 15, 1993. As a result, this environmental assessment has been prepared using the abbreviated format provided in 21 CFR §25.31a(b)(3) which specifies that Items 7 through 11 are not included.

ITEM 12. List of Preparers:

Daniel M. Woltering, Ph.D., Principal, ENVIRON International Corporation, Arlington, Virginia. Twenty years of experience in ecotoxicology and environmental risk assessment.

Eric M. Silberhorn, Ph.D., Senior Associate, ENVIRON International Corporation, Arlington, Virginia. Fourteen years of experience in ecotoxicology, environmental science, and ecological risk assessment.

George P. Grandolfi, Ph.D., Associate Director, Formulation Development, Cephalon, Inc., West Chester, Pennsylvania. Eight years of experience in pharmaceutical formulation research and development.

ITEM 13. Certification:

The undersigned Cephalon®, Inc. official certifies that the information presented is true, accurate, and complete to the best of the knowledge of the preparers of the environmental assessment.

The undersigned official certifies that the environmental assessment summary document (pages 1-8) contains non-confidential information and acknowledges that this information will be made available to the public in accordance with 40 CFR §1506.6.



Douglas Clafey
Associate Director, Quality Assurance

Date 5/1/97

ITEM 14. References:

None

ITEM 15. Appendices:

- Appendix A: Identification of Chemical Substances in Modafinil Tablets (CONFIDENTIAL)
- Appendix B: Contract Manufacturer - Key Intermediate: Facility Information and Compliance Statement (CONFIDENTIAL)
- Appendix C: Contract Manufacturer - Drug Substance: Facility Information and Compliance Statement (CONFIDENTIAL)
- Appendix D: Contract Manufacturing Facility - Drug Product: Certification of Compliance (NON-CONFIDENTIAL)
- Appendix E: Contract Manufacturing Facility - Drug Product: Applicable Regulations and Environmental Permits (CONFIDENTIAL)
- Appendix F: Contract Disposal Facility - Drug Product: Facility Location and Applicable Permits (CONFIDENTIAL)
- Appendix G: Material Safety Data Sheet for Modafinil Drug Substance (NON-CONFIDENTIAL)
- Appendix H: Maximum Yearly Market Volume Estimate for Modafinil Tablets (CONFIDENTIAL)

D-1

APPENDIX D:

Contract Manufacturing Facility - Drug Product:

Certification of Compliance

(NON- CONFIDENTIAL)

054



CIRCA PHARMACEUTICALS, INC.

33 RALPH AVENUE P.O. BOX 30 COPENHAGEN, NY 11726-0030
(516) 842-8383 FAX (516) 842-8630

Circa Pharmaceuticals, Inc. hereby certifies that it is in compliance with, or on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees and administrative orders applicable to the production of modafinil at our facilities in Copiague, New York as well as emission requirements set forth in applicable federal, state, and local statutes and regulations applicable to the production of modafinil at its facilities in Copiague, New York. Approval and subsequent manufacture of production quantities of this drug product are not expected to affect this compliance.

 3/7/96

Moez Kakal

Date

Director, Quality Assurance

G-1

APPENDIX G:

**Material Safety Data Sheet
for Modafinil Drug Substance**

(NON-CONFIDENTIAL)

056



Cephalon, Inc.

Material Safety Data Sheet

Section 1 - Chemical Product and Company Identification

Manufacturer Name & Address: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380

Emergency Phone Number: (800) 424-9300

Phone Number for Information: (610) 344-0200

Prepared By: S. Field, J. Mallamo, J. Patterson, D. Stong

Date Prepared: 12/96

Substance: 2-[(diphenylmethyl) sulfinyl] acetamide, 2-(benzhydrylsulfinyl) acetamide

Other Designation (e.g., synonyms, trade names): modafinil, PROVIGIL®, CEP 1538

Chemical Family: Acetamide

Section 2 - Composition and Information On Ingredients

Component(s): 2-[(diphenylmethyl) sulfinyl] acetamide, 2-(benzhydrylsulfinyl) acetamide

CAS Number(s): 68693-11-8

Percentage(s): > 99%

Other Hazard Ingredients: none

Section 3 - Hazards Identification

Potential Health Effects

Primary Entry Routes: Inhalation, ingestion

Target Organs:

Inhalation

Short Term Effects: data not available

Long Term Effects: data not available

Skin Contact

Short Term Effects: data not available

Long Term Effects: data not available

Eye Contact

Short Term Effects: data not available

Long Term Effects: data not available

Ingestion

Short Term Effects: Rodent oral LD₅₀ > 1000 mg/kg, Dog oral LD₅₀ > 200 mg/kg

Long Term Effects: Non-toxic to rats at 20 mg/kg/day and dogs at 10 mg/kg/day

Parenteral Contact

Short Term Effects: data not available

Long Term Effects: data not available

Carcinogen Status

(answer yes, no or not applicable)

OSHA (regulated carcinogen): no

NTP (confirmed or suspect): no

IARC(1, 2A or 2B): no

Medical Conditions Aggravated by Long-Term Exposure: data not available

Other: N/A

Section 4 - First Aid Measures

Inhalation: Remove from exposure area to fresh air. If breathing has stopped, perform artificial respiration. Contact physician immediately.

Skin Contact: Wash with copious amounts of water or soap and water. Contact physician immediately.

Eye Contact: Flush eyes with copious amounts of water or normal saline. Contact physician immediately.

Ingestion: Induce vomiting. (Keep head lower than hips to prevent aspiration). Contact physician immediately.

Note to Physician (i.e., specific medical info. on treatment & diagnostic procedures): data not available

Antidote: data not available

Section 5 - Fire Fighting Measures

Fire and Explosion Hazard: N/A

Extinguishing Media: Dry chemical, carbon dioxide, water spray, foam

Flash Point: N/A

Lower Flammable Limit: N/A

Upper Flammable Limit: N/A

Autoignition Temperature: N/A

Flammability Class (OSHA): N/A

Hazardous Combustion Products: data not available

Section 6 - Accidental Release Measures

Indoor Spill: use wet methods to prevent airborne dusts. Remove residue with HEPA-equipped vacuum.

Release into Soil: data not available

Release/Discharge into Ambient Air: data not available

Release/Discharge into Groundwater/Waterways/Sewers: data not available

Section 7 - Handling and Storage

Handling Precautions: The effects of occupational exposure to this product are unknown.

Handle as potentially hazardous material using traditional industrial hygiene methods.

Storage Requirements: Store at ambient temperatures, below 40 degrees Celcius.

Section 8 - Exposure Controls and Personal Protection

Exposure Limits: not defined

Ventilation: Local exhaust, mechanical

Eye Protection: safety glasses

Clothing: Body covering clothing to prevent contact with skin.

Gloves: for handling dry powder, use nitrile or other suitable disposable glove. When handling solutions, select glove based on solvent.

Respiratory Protection: NIOSH-certified negative air-purifying respirator with HEPA cartridges. If airborne concentration is unknown or suspected to exceed the respirator's maximum use concentration, select a respirator with a higher protection factor.

For Firefighting and Other Immediately Dangerous to Life or Health Conditions:

Self-contained breathing apparatus in pressure-demand mode, and personal protective clothing suitable to prevent dermal exposure

Section 9 - Physical and Chemical Properties

Description: White, crystalline powder. Odorless.

Molecular Weight: 273.35

Molecular Formula: C₁₂H₁₄NO₅S

Boiling Point: N/A
Freezing Point: N/A
Melting Point: melts with decomposition between 165°-170°
Vapor Pressure (mm Hg): N/A
Density (H₂O=1 at 4°C): N/A
Saturated Vapor Density (air=1): 0.4
Specific Gravity (H₂O=1): N/A
Water Solubility: 0.4 mg/mL
Percent Volatiles by Volume: < 0.1%
pH: N/A
Odor Threshold: N/A
Evaporation Rate (Butyl Acetate = 1): N/A
Viscosity: N/A
Other Solubilities (e.g., solvents, salt solutions): methanol 13.0 g/L, acetone 5.0 g/L, ethanol 2.5 g/L, isopropanol 0.5 g/L, DMSO > 100 g/L, cyclohexane < 0.1 g/L

Section 10 - Stability and Reactivity

Stability/Reactivity: very stable as a solid
Conditions to Avoid: in acid or basic solution, Modafinil forms Modafinil-acid
Incompatibilities: unknown
Hazardous Decomposition: not anticipated to occur
Polymerization: not observed, not anticipated to occur

Section 11 - Toxicological Information

Acute and Chronic Studies
Inhalation: data not available
Ingestion: Rodent oral LD₅₀ > 1000 mg/kg, Dog oral LD₅₀ > 200 mg/kg
Non-toxic to rats at 20 mg/kg/day and dogs at 10 mg/kg/day
Skin: data not available
Eye: data not available
At Increased Risk from Exposure: data not available
Additional Data: N/A

Section 12 - Ecological Information

Ecotoxicity (i.e., acute & chronic toxicity to fish, plants and microorganisms): data not available
Chemical Behavior in the Air, Soil or Water (i.e., persistence, degradation, soil mobility, bioaccumulation and photolytic stability): data not available

Section 13 - Disposal Considerations

Disposal Methods: Incinerate under controlled conditions to prevent dust explosions. Dispose in compliance with applicable federal, state, and local laws and regulations.
Waste Minimization (i.e., recycling or reclamation): data not available
Limitations Per Federal, State or Local Regulations: N/A

Section 14 - Transport Information

Is the chemical regulated by the U.S. Department of Transportation (DOT)? No (exemptions apply for certain quantities; classify as ORM-D)
Shipping Name and Identification Number: Toxic solid, organic, n.o.s. (medicines)
DOT Hazard Class or Division: 6.1
DOT Packing Group: III
DOT Labeling Requirements: UN NA2811
DOT Packaging Authorizations: N/A
DOT Quantity Limitations: 30 kg for consumer commodity exemption

Section 15 - Regulatory Information

TSCA Status: N/A
CERCLA Section 103 (40 CFR 302.4): N/A
SARA Section 302 (40 CFR 355.30): N/A
SARA Section 304 (40 CFR 355.40): N/A
SARA Section 313 (40 CFR 372.65): N/A
OSHA Process Safety (29 CFR 1910.119): N/A
California Proposition 65: N/A
Sara Hazard Categories, SARA Sections 311/312 (40 CFR 370.21)
Acute Hazard: N/A
Chronic Hazard: N/A
Fire Hazard: N/A
Reactivity Hazard: N/A

Section 16 - Other Information

References: available upon request

Cephalon, Inc. provides this information in good faith based upon best available knowledge. The effects of occupational exposure to the compound described in this MSDS are not known. Individuals receiving this information are encouraged to consult with appropriate professionals as necessary prior to use, storage and/or disposal of this compound, and for evaluating its appropriateness for their particular application(s). Cephalon, Inc. does not represent that this MSDS is all-inclusive and notes that this MSDS shall be used only as a guide.