CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 20-785

Chemistry Review(s)

DIVISION OF DERMATOLOGICAL AND DENTAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-785 **CHEM.REVIEW #:** 2 **REVIEW DATE:** 9-Jul-98

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
CMC presubmission (16 volumes)	24-Oct-96	24-Oct-96	Chem. Rev. #1
ORIGINAL	20-Dec-96	20-Dec-96	Chem. Rev. #1
fax	16-Jan-97	16-Jan-97	Chem. Rev. #1
BZ	23-Jan-97	23-Jan-97	Chem. Rev. #1
BM	3-Feb-97	3-Feb-97	Chem. Rev. #1
BC	25-Feb-97	26-Feb-97	Chem. Rev. #1
BZ	7-Mar-97	7-Mar-97	Chem. Rev. #1
BZ	1-Apr-97	1-Apr-97	Chem. Rev. #1
BC	12-Jun-97	12-Jun-97	Chem. Rev. #1
BC	21-Aug-97	21-Aug-97	Chem. Rev. #1
NC	27-Aug-97	28-Aug-97	Chem. Rev. #1
fax	28-Aug-97	28-Aug-97	Chem. Rev. #1
NC	2-Sep-97	3-Sep-97	Chem. Rev. #1
BC	18-Sep-97 (vol. 18.1)	18-Sep-97	19-Sep-97
BL	21-Oct-97 (vol. 20.1)	21-Oct-97	22-Oct-97
BC	27-Oct-97 (vol. 21.1)	27-Oct-97	27-Oct-97
BC	14-Nov-97 (vol. 23.1)	14-Nov-97	17-Nov-97
BC	2-Jan-98 (vol. 26.1)	2-Jan-98	2-Jan-98
BL	20-Jan-98 (vol. 31.1)	20-Jan-98	20-Jan-98
AZ	26-Jan-98	27-Jan-98	no chem. assignment
BC	24-Mar-98	24-Mar-98	27-Mar-98
BC	19-Jun-98	19-Jun-98	20-Jun-98

NAME & ADDRESS OF APPLICANT: Celgene Corp.
7 Powder Horn Drive
Warren, NJ 07059

DRUG PRODUCT NAME

Proprietary:	Thalomid Capsules
Nonproprietary/USAN:	Thalidomide
Code Names/#'s:	none
Chemical Type/ Therapeutic Class:	1 P

ANDA Suitability Petition/DESI/Patent Status:
N/A

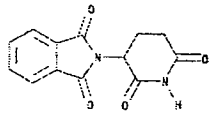
PHARMACOLOGICAL CATEGORY/INDICATION:

Erythema nodosum leprosum

DOSAGE FORM: Capsule
STRENGTHS: 50 mg
ROUTE OF ADMINISTRATION: Oral
DISPENSED: XX **Rx** ___ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.:

m.w. 258.23
CAS Registry No. 50-35-1
$C_{13}H_{10}N_2O_4$
N-(2,6-dioxo-3-piperidyl)phthalimide



SUPPORTING DOCUMENTS:

Document Type & Number	Subject	Holder	Status	Review Date	Letter Date
DMF —	[redacted]		DE IR	10/31/97 3/10/98	11/4/97 3/10/98
DMF —	[redacted]		AE RR	3/2/97 2/17/98	2/20/98
IND 11,359	thalidomide	Gillis W. Long Hansen's Disease Center, Carrville, LA	AT	#1: 7-Jul-90 #2: 11-Nov-95 #3: 27-Nov-95	n/a
IND 48,177	thalidomide capsules	Celgene	AT		n/a
IND —	thalidomide capsules	Celgene	AT	3-Mar-94 (Jarski/HFD-590)	n/a

RELATED DOCUMENTS (if applicable):

None

CONSULTS:

Labeling and Nomenclature Committee Review; review dated 18-Feb-98 attached as Appendix #1; see comments under item F of the Review Notes

REMARKS/COMMENTS:

An approvable (AE) letter was issued 19-Sep-97. As of the date of this review, responses have been received to all deficiencies. The PDUFA goal date is July 27, 1998. The contents of the responses are briefly noted as follows:

- 18-Sep-97 (BC): revision of bulk drug assay specification
- 21-Oct-97 (BL): labeling (package insert, "early draft"); initially classified as "AC", revised to "BC" because response was incomplete
- 27-Oct-97 (BC): response to AE letter, CMC issues 1-3 & 6 from 19-Sep-97 AE letter
- 14-Nov-97 (BC): packaging material and stability (blister pack)
- 2-Jan-98 (BC): revision to EA (withdrawal)
- 20-Jan-98 (BL): labeling (blister pack and carton mock-up)
- 24-Mar-98 (BC): stability update for drug product, drug substance, and intermediate
- 19-Jun-98 (BC): method validation packages

Proposed Phase 4 CMC Commitments		
Subject	**Description**	**Suggested Due Date Post-Approval**
Description (bulk)	Determination of solubility of thalidomide in [ ] media	six months
Synthesis	Development of [ ]	COMPLETED 10/27/97
Process Controls	Stability study [ ]	COMPLETED 3/24/98
Specifications and Methods (drug product)	Develop a test/specification for the packaged drug product to verify the integrity of the blister pack with respect to moisture vapor transmission	one year

Proposed Phase 4 CMC Commitments		
Subject	**Description**	**Suggested Due Date Post-Approval**
Packaging components	Testing to verify the claimed moisture vapor transmission rate for the packaging components	six months
Stability	Update of stability data for lots DEV 2775, 2800 and 2811	November, 1998

The commitments noted above, as well as other review issues, were discussed with the Applicant in a telephone conference on 12-Mar-98 (Steve Thomas, Dave Sterling, Norma Loeffler and Alison Smith, Celgene and Mary Jane Walling and Wilson DeCamp, FDA, participating). See below and Appendix #2 for the specific items that were discussed.

CONCLUSIONS & RECOMMENDATIONS:

The following comments are to be directed to the applicant:

1. As a post-approval (phase 4) commitment, please commit to submission of the results of release testing results for lots 0091N, 0092N and 0149N, along with updated stability data for lots DEV 2775, 2800 and 2811. These results, along with previously submitted stability data on the drug substance, will be used to evaluate the bulk drug and finished product specifications.
2. As a post-approval (phase 4) commitment, please develop and propose a component qualification test for the packaged drug product that will verify the integrity of the blister pack with respect to moisture vapor transmission. This should not be considered to be a regulatory specification.
3. DMFs [redacted] are not current; this will not be an approvability issue.
4. The outstanding phase 4 commitments 5(a) and 5(e) (see AE letter, 19-Sep-97] should be brought to the attention of the applicant.
5. Please submit typical COA's for the blister package components.
6. Please commit to testing the existing packaging component inventory (or the next batch obtained) to verify the claimed moisture vapor transmission rate for the components.

7. A methods validation package should be assembled, including the CMC summary, and the appendices and attachments noted under Item E of the Review Notes (submitted 19-Jun-98).
8. We recommend that the printing on the foil back of the blister pack be revised to include the logo and pregnancy warning, and to appear associated with each capsule.
9. We note that a single carton contains the equivalent of six weeks supply at the lowest dosage rate (100 mg/day). This seems to be counter to the stated intent of dispensing no more than a four week supply at one time.

Items 2-9 in the above list are not approvability issues. They have previously been communicated to the applicant as information requests, and do not need to be included in an action letter.

An APPROVAL action is recommended for manufacturing and controls under section 505 of the Act. All manufacturing facilities are in acceptable GMP compliance as of July 14, 1997 (see review #1, item G., Establishment Inspections). An approval action may be issued on or before July 14, 1998.

Wilson H. DeCamp, Ph.D.
Chemistry Team Leader

Attachments:
(1) L&NC tradename consult, 2/18/98
(2) Memoranda of Telecons (a) 3/12/98; (b) 6/16/98; (c) 7/7/98

cc: Orig. NDA 20-785
HFD-540/Division File
HFR-MA350/NWJ-DO
HFR-SW350/KAN-DO
HFD-540/DeCamp
HFD-540/Vaughan
HFD-540/O'Connell
HFD-540/Hill
HFD-540/Bashaw

HFD-540/Gao
HFD-540/White
HFD-830/Chen
HFD-102/Sheinin
R/D Init by: Chen arc 7/9/98
filename: **N20785.RV2**

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____ § 552(b)(5) Deliberative Process

____ § 552(b)(4) Draft Labeling

Appendix #1

Labeling and Nomenclature Committee Review

Consult #880 (HFD-540)

THALOMID

thalidomide capsules

The Committee would usually object to a brand name containing so much of the generic name in it however, this is a very special drug that either should not have a proprietary name or should have a brand name that strongly identifies the drug substance.

The committee finds the proposed brand name acceptable given the special history and toxicity of this drug.

P Uberling 2/18/98
, Chair
CDER Labeling and Nomenclature Committee

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____ § 552(b)(5) Deliberative Process

____ § 552(b)(4) Draft Labeling

CDER Establishment Evaluation Report
for August 05, 1997

Application: **NDA 20785/000**
Stamp: **20-DEC-1996** Regulatory Due: **20-SEP-1997**
Applicant: **CELGENE**
7 POWDER HORN DR
WARREN, NJ 07059

Priority: **1P** Org Code: **540**
Action Goal: District Goal: **01-SEP-1997**
Brand Name: **SYNOVIR (THALIDOMIDE) 50MG CAP**
Established Name:
Generic Name: **THALIDOMIDE**
Dosage Form: **CAP (CAPSULE)**
Strength: **50 MG**

FDA Contacts: **W. DECAMP II (HFD-540) 301-827-2041 , Review Chemist**
C. CHEN (HFD-830) 301-827-2001 , Team Leader

Overall Recommendation:

ACCEPTABLE on 14-JUL-1997 by M. EGAS (HFD-322) 301-594-0095

Establishment: [

DMF No:

AADA No:

]

Profile: **NEC** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 09-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities:
[ ]

Establishment: **2248779**
CELGENE CORP
7 POWDER HORN DR
WARREN, NJ 07059

DMF No:

AADA No:

Profile: **NEC** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 11-JUL-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:
DRUG SUBSTANCE OTHER TESTER
FINISHED DOSAGE OTHER TESTER

Establishment: [

DMF No:

AADA No:

]

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 14-JUL-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:
[ ]

Establishment: [

DMF No:

]

[ ] AADA No:

[ ] Responsibilities:
[ ]

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 10-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [ ] DMF No:

AADA No:
[ ]

Profile: **NEC** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 11-MAR-1997** [ ]
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: [ ] DMF No:

AADA No:
[ ]

Profile: **NEC** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 09-JAN-1997** [ ]
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [ ] DMF No:

AADA No:
[ ]

Profile: **CSG** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 09-JAN-1997** [ ]
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [ ] DMF No:

AADA No:
[ ]

Profile: **CSG** OAI Status: **NONE** Responsibilities:

Last Milestone: **OC RECOMMENDAT 13-MAR-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: [redacted]

DMF No:

AADA No:

Profile: **NEC** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 09-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: [redacted]

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On Original

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___ § 552(b)(4) Draft Labeling

SEP 8 1997

DIVISION OF DERMATOLOGICAL AND DENTAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-785 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 6-Sep-97

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
CMC presubmission (16 volumes)	24-Oct-96	24-Oct-96	25-Oct-96
ORIGINAL	20-Dec-96	20-Dec-96	20-Dec-96
fax	16-Jan-97	16-Jan-97	16-Jan-97
BZ	23-Jan-97	23-Jan-97	29-Jan-97
BM	03-Feb-97	03-Feb-97	06-Mar-97
BC	25-Feb-97	26-Feb-97	05-Mar-97
BZ	07-Mar-97	07-Mar-97	07-Mar-97
BZ	01-Apr-97	01-Apr-97	01-Apr-97
BC	12-Jun-97	12-Jun-97	12-Jun-97
BC	21-Aug-97	21-Aug-97	22-Aug-97
NC	27-Aug-97	28-Aug-97	28-Aug-97
fax	28-Aug-97	28-Aug-97	28-Aug-97
NC	02-Sep-97	03-Sep-97	03-Sep-97

NAME & ADDRESS OF APPLICANT: Celgene Corp.
7 Powder Horn Drive
Warren, NJ 07059

DRUG PRODUCT NAME

Proprietary:	Synovir Capsules
Nonproprietary/USAN:	Thalidomide
Code Names/#'s:	none
Chemical Type/ Therapeutic Class:	**1 P**

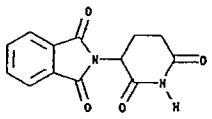
ANDA Suitability Petition/DESI/Patent Status:
N/A

PHARMACOLOGICAL CATEGORY/INDICATION:
Erythema nodosum leprosum

DOSAGE FORM:	Capsule
STRENGTHS:	50 mg
ROUTE OF ADMINISTRATION:	Oral
DISPENSED:	XX **Rx** _____ **OTC**

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.:

m.w. 258.23
CAS Registry No. 50-35-1
$C_{13}H_{10}N_2O_4$
N-(2,6-dioxo-3-piperidyl)phthalimide



SUPPORTING DOCUMENTS:

IND 11,359, thalidomide, Gillis W. Long Hansen's Disease Center, Carrville, LA; letter of authorization dated June 29, 1993, signed by Robert C. Hastings, M.D., Ph.D.
IND 48,177, thalidomide capsules, Celgene
IND [ ] thalidomide capsules, Celgene

RELATED DOCUMENTS (if applicable):

Fax, Celgene to HFD-540, 1/16/97 (12 pages); attached as Appendix 1(a) (full copies filed in NDA 20-785 only)
Fax, [ ] to HFD-540, 3/12/97 (8 pages); attached as Appendix 1(b) (full copies filed in NDA 20-785 only)
Fax, [ ] to HFD-540, 3/17/97 (11 pages; cover sheet missing); attached as Appendix 1(c) (full copies filed in NDA 20-785 only)
[ ] dates of inspection 7/7-7/8/97, dated 7/11/97; attached as Appendix 2 with exhibits (full copies filed in NDA 20-785 only)
EIR, NWK-DO, Celgene Corp.; dates of inspection 2/24-2/28/97, dated 4/8/97; attached as Appendix 3 without exhibits (full copies filed in NDA 20-785 only)
[ ] dates of inspection 11/11-11/14/96, dated 1/17/97; attached as Appendix 4 (full copies filed in NDA 20-785 only)
EES report, dated 8/5/97; attached as Appendix 5; see comments under item G of Review Notes

CONSULTS:

Statistical evaluation of stability data, 4/1/97 and 6/12/97 submissions; review dated 8/6/97 and addendum dated 8/8/97; attached as Appendix 6; see comments under item B.9 of Review Notes

Environmental assessment, 96/10/24, to Nancy Sager, HFD-357; review and comments received 12/13/96; review attached as Appendix 7; see draft comments under item D of the Review Notes

Labeling and Nomenclature Committee Review; review attached as Appendix 8; see comments under item F of the Review Notes

REMARKS/COMMENTS:

The original PDUFA goal date of June 20, 1997, was extended by a major amendment received June 16. The extended PDUFA goal date is September 20, 1997.

The amendment (BZ) dated January 23, 1997 (Vol. 3.1), is a complete resubmission of the summary volume originally submitted December 20, 1996.

The amendment (BM) dated February 3, 1997 (Vol. 4.1), includes revised draft labeling on pp. 223-230. Draft or mock-up container labels and cartons are not included.

The amendment (BC) dated February 25, 1997 (Vol. 5.1), includes a statistical trend analysis of the stability data through [ ]. These data were updated in the amendment (BZ) dated April 1, 1997, which also included a SAS diskette. These submissions have been referred for statistical review, since the proposed expiry substantially exceeds the data available.

The amendment (BZ) dated March 7, 1997, includes a copy of the draft labeling in diskette form.

The amendment (BC) dated June 12, 1997 (Vols. 10.1-10.2), is an update of the synthetic procedure, a revision of the dissolution method, and a further update of the stability data.

The correspondence (NC) dated August 27, 1997, provided supporting information about the assay history of [ ] development lots of bulk thalidomide, plus drug substance and drug product release data for two process validation batches.

The correspondence (NC) dated September 3, 1997, submitted Celgene's SOP for analysis of duplicate assay values. This is not for review, but supports the procedures described in item A.6.A., below.

The great majority of the clinical data submitted in this application originated in the use of thalidomide under IND 11,359. The drug product used under this IND originated from multiple sources, mostly foreign, and included both capsules and tablets. See additional comments under Drug Product, Manufacturers (Review Notes, item B.4., below). There is little, if any, manufacturing information about any of the sources. The quality assurance of these imported lots was derived from analytical testing procedures developed at the Division of Drug Analysis (HFH-300), and which resulted in the monographs incorporated in this application as Vol. 1.2, Appendix 3.3. Analytical testing was performed at DDA and at NOL-DL (HFR-SE460). With a single exception, all the imported lots were found to meet the provisional specifications of the DDA monograph. In that case, the lot was found to fail the provisional dissolution specification; it was permitted to be used under the IND with special instructions that the tablets were to be crushed before administering.

This application includes a bioequivalence study comparing the Celgene product with one lot of imported thalidomide. This study is reviewed in the Clinical Pharmacology/Biopharmaceutics Review, dated August 13, 1997. This study compared two different Celgene formulations of thalidomide capsules with one lot of product imported from Tortuga. The lot number appears to be 001. According to information submitted by fax on August 28, 1997, this lot was 001/94, and the source was [redacted]. See Item D, Investigational Formulations, for additional information.

A meeting of the Dermatological and Ophthalmic Drugs Advisory Committee was held on September 4-5, 1997, to discuss this application. Certain comments voiced at that meeting are mentioned below and in the Review Notes.

CONCLUSIONS & RECOMMENDATIONS:

The application is APPROVABLE for manufacturing and controls under section 505 of the Act. All manufacturing facilities are currently in acceptable GMP compliance as of July 14, 1997 (see item G., Establishment Inspections). An approval action may be issued on or before July 14, 1998.

Two issues of potential approvability should be communicated to the Applicant: a request to tighten the proposed drug substance specifications to the limits of the DDA monograph and a request to decrease the expiration dating to eighteen months. Labeling revisions will also need to be communicated.

It has yet to be determined whether a categorical exclusion can be claimed for this product under the new EA regulations (see *Federal Register*, July 29, 1997, pp. 40570-40600; effective date August 28, 1997).

Specific items for which additional information is requested appear under several items. In each case, the request for information does not affect the overall approvability of the application. Additional information requests are identified under the following headings: Drug Substance [Description and Characteristics, Synthesis, Specifications and Methods], Drug Product [Specifications and Methods (drug product), Container/Closure System, Stability], Environmental Assessment, Methods Validation, and Labeling.

Wilson H. DeCamp, Ph.D.
Chemistry Team Leader

Attachments (9)
(1) Memorandum of Telecon, 8/30/97
(2-9) Appendices 1-8

cc: Orig. NDA 20-785 (with all attachments)
following copies distributed with attachment 1 and appendices 5-8 only
HFD-540/Division File
HFR-MA350/NWJ-DO

[ ]
remaining copies distributed without attachments
HFD-540/DeCamp
HFD-540/Vaughan
HFD-540/O'Connell
HFD-540/Hill
HFD-540/Bashaw
HFD-540/Gao
HFD-540/White
HFD-830/Chen
HFD-102/Sheinin
R/D Init by: Chen CMC 9/8/97
filename:
N20785.RVX

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___ § 552(b)(4) Draft Labeling

CDER Establishment Evaluation Report
for August 05, 1997

Application: **NDA 20785/000**
Stamp: **20-DEC-1996** Regulatory Due: **20-SEP-1997**
Applicant: **CELGENE**
7 POWDER HORN DR
WARREN, NJ 07059

Priority: **1P** Org Code: **540**
Action Goal: District Goal: **01-SEP-1997**
Brand Name: **SYNOVIR (THALIDOMIDE) 50MG CAP**
Established Name:
Generic Name: **THALIDOMIDE**
Dosage Form: **CAP (CAPSULE)**
Strength: **50 MG**

FDA Contacts: **W. DECAMP II (HFD-540) 301-827-2041 , Review Chemist**
C. CHEN (HFD-830) 301-827-2001 , Team Leader

Overall Recommendation:

ACCEPTABLE on 14-JUL-1997 by M. EGAS (HFD-322) 301-594-0095

Establishment: [illegible]
DMF No:
AADA No:

Profile: **NEC** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 09-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities:
[illegible]

Establishment: **2248779**
CELGENE CORP
7 POWDER HORN DR
WARREN, NJ 07059
DMF No:
AADA No:

Profile: **NEC** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 11-JUL-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:
DRUG SUBSTANCE OTHER TESTER
FINISHED DOSAGE OTHER TESTER

Establishment: [illegible]
DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 14-JUL-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities:
[illegible]

Establishment: [illegible]
DMF No:

[redacted] AADA No:

[redacted] Responsibilities:
[redacted]

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDAT 10-JAN-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [redacted] DMF No:

AADA No:

[redacted]

Profile: **NEC** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 11-MAR-1997** [redacted]
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: [redacted] DMF No:

AADA No:

[redacted]

Profile: **NEC** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 09-JAN-1997** [redacted]
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [redacted] DMF No:

AADA No:

[redacted]

Profile: **CSG** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 09-JAN-1997** [redacted]
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [redacted] DMF No:

AADA No:

[redacted]

Profile: **CSG** OAI Status: **NONE** Responsibilities:

Last Milestone: **OC RECOMMENDAT 13-MAR-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: [redacted] DMF No:

AADA No:

Profile: **NEC** OAI Status: **NONE** Responsibilities:
Last Milestone: **OC RECOMMENDAT 09-JAN-1997** [redacted]
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

CDER Establishment Evaluation Report
for July 14, 1998

Application: **NDA 20785/000**
Stamp: **20-DEC-1996** Regulatory Due: **27-JUL-1998**
Applicant: **CELGENE**
7 POWDER HORN DR
WARREN, NJ 07059

Priority: **1P** Org Code: **540**
Action Goal: District Goal: **01-SEP-1997**
Brand Name: **THALIDOMIDE 50MG CAPSULES**
Established Name:
Generic Name: **THALIDOMIDE**
Dosage Form: **CAP (CAPSULE)**
Strength: **50 MG**

FDA Contacts: **W. DECAMP II (HFD-540) 301-827-2041 , Review Chemist**
C. CHEN (HFD-830) 301-827-2001 , Team Leader

Overall Recommendation:

ACCEPTABLE on 14-JUL-1998 by M. EGAS (HFD-322) 301-594-0095
ACCEPTABLE on 14-JUL-1997 by M. EGAS (HFD-322) 301-594-0095

Establishment: C
DMF No:
AADA No:

J

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: C

J

Establishment: **2248779**
CELGENE CORP
7 POWDER HORN DR
WARREN, NJ 07059

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON FILE REVIEW**

Responsibilities: **DRUG SUBSTANCE OTHER TESTER**
FINISHED DOSAGE OTHER TESTER

Establishment: C

DMF No:
AADA No:

J

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**

Responsibilities: C

J

Reason: **BASED ON PROFILE**

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CSG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: [redacted]

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: [redacted]

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: [redacted]

Establishment: [redacted]

DMF No:
AADA No:

Profile: **CSG** OAI Status: **NONE**

Responsibilities: [redacted]

Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: [redacted] DMF No:
AADA No:

Profile: **CSG** OAI Status: **NONE** Responsibilities: [redacted]
Last Milestone: **OC RECOMMENDATION**
Milestone Date **14-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON FILE REVIEW**
DISTRICT RECOMMENDATION

Establishment: [redacted] DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE** Responsibilities: [redacted]
Last Milestone: **OC RECOMMENDATION**
Milestone Date **13-JUL-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

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109 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

____ § 552(b)(5) Deliberative Process

____ § 552(b)(4) Draft Labeling

Appendix #8
Labeling and Nomenclature Committee Review

Consult #831 (HFD-540)

SYNOVIR thalidomide capsules

The Committee noted numerous potential look-alike/sound-alike conflicts with the proposed brand name: SYNACORT, SYNALAR, SYNEMOL, SINEQUAN, SINEMET and CINOBAC. Additionally, "-vir" is the USAN stem reserved for anti-viral products and the pending product is not an anti-viral. The Committee recommends against the use of USAN syllables in proprietary names and especially the inappropriate use of stem syllables.

Given the large number of potential conflicts and the misleading use of "-vir', the Committee finds the proposed proprietary name unacceptable.

DUBoring 8/8/97, Chair
CDER Labeling and Nomenclature Committee

REQUEST FOR TRADEMARK REVIEW

831

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461

From: Division of Dermatologic and Dental Drug Products	**HFD-540**
Attention: Wilson H. DeCamp, Ph.D. WDD 6/20/97	**Phone:** (301) 827-2041
Date: June 20, 1997	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademark: Synovir	**NDA/ANDA#** NDA 20-875
Established name, including dosage form: thalidomide capsules	
Other trademarks by the same firm for companion products: none	
Indications for Use (may be a summary if proposed statement is lengthy): erythema nodosum leprosum (an inflammatory reaction occurring in patients with Hansen's disease	
Initial Comments from the submitter (concerns, observations, etc.): (1) note the use of the suffix "-vir"; this may suggest anti-viral activity (e.g., the established names acyclovir, ganciclovir, etc.) (2) many (but not all) of the trade names beginning with "Syn-" are used by Syntex (now merged with Hoffman-La Roche) (3) multiple IND's use this product in AIDS-related conditions, especially AIDS wasting syndrome; off-label use is likely; C J	

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

cc: Original NDA 20-875; HFD-540/division file; HFD-540/K.D.White; HFD-540/DeCamp

Rev. December 95

11 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

___ § 552(b)(5) Deliberative Process

___ § 552(b)(4) Draft Labeling