CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204026Orig1s000

CHEMISTRY REVIEW(S)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application:	NDA 204026/000	**Sponsor:**	CELGENE
Org. Code:	161		86 MORRIS AVE
Priority:	1		SUMMIT, NJ 07901
Stamp Date:	10-APR-2012	**Brand Name:**	Pomalidomide
PDUFA Date:	10-FEB-2013	**Estab. Name:**	
Action Goal:		**Generic Name:**	Pomalidomide
District Goal:	11-AUG-2012	**Product Number; Dosage Form; Ingredient; Strengths**	001; CAPSULE; POMALIDOMIDE; 1MG 002; CAPSULE; POMALIDOMIDE; 2MG 003; CAPSULE; POMALIDOMIDE; 3MG 004; CAPSULE; POMALIDOMIDE; 4MG

FDA Contacts:				
	J. MARTIN	Project Manager	(HFV-530)	3017962072
	G. LADOUCEUR	Review Chemist	(HFD-800)	3017963878
	J. BROWN	Team Leader		3017961652

Overall Recommendation:	ACCEPTABLE	on 24-JAN-2013	by T. SHARP	()	3017963208
	PENDING	on 17-APR-2012	by EES_PROD		
	PENDING	on 17-APR-2012	by EES_PROD		
	PENDING	on 17-APR-2012	by EES_PROD		

Establishment:	**CFN:** (b) (4)	**FEI:** (b) (4)	
	(b) (4)		
DMF No:		**AADA:**	
Responsibilities:	DRUG SUBSTANCE MANUFACTURER		
	DRUG SUBSTANCE RELEASE TESTER		
Profile:	(b) (4)	**OAI Status:**	NONE
Last Milestone:	OC RECOMMENDATION		
Milestone Date:	23-APR-2012		
Decision:	ACCEPTABLE		
Reason:	DISTRICT RECOMMENDATION		

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Establishment: **CFN:** 2248779 **FEI:** 3004991673

CELGENE CORP

SUMMIT, , UNITED STATES 07901

DMF No: **AADA:**

Responsibilities: FINISHED DOSAGE STABILITY TESTER

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

Last Milestone: OC RECOMMENDATION

Milestone Date: 02-AUG-2012

Decision: ACCEPTABLE

Reason: BASED ON PROFILE

Establishment: **CFN:** **FEI:** 3006323509

CELGENE INTERNATIONAL SARL
ROUTE DE PERREUX 1

BOUDRY, , SWITZERLAND

DMF No: **AADA:**

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE RELEASE TESTER

Profile: CAPSULES, PROMPT RELEASE **OAI Status:** NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 21-SEP-2012

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

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

(b) (4)

DMF No: **AADA:**

Responsibilities: DRUG SUBSTANCE MANUFACTURER

DRUG SUBSTANCE RELEASE TESTER

Profile: (b) (4) **OAI Status:** NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 23-APR-2012

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

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

(b) (4)

DMF No: **AADA:**

Responsibilities: FINISHED DOSAGE MANUFACTURER

FINISHED DOSAGE RELEASE TESTER

Profile: CAPSULES, PROMPT RELEASE **OAI Status:** NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 24-JAN-2013

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

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

(b) (4)

DMF No: **AADA:**

Responsibilities: FINISHED DOSAGE PACKAGER

Profile: CAPSULES, PROMPT RELEASE **OAI Status:** NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 18-APR-2012

Decision: ACCEPTABLE

Reason: BASED ON PROFILE

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

(b) (4)

DMF No: **AADA:**

Responsibilities: DRUG SUBSTANCE STABILITY TESTER

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

Last Milestone: OC RECOMMENDATION

Milestone Date: 18-APR-2012

Decision: ACCEPTABLE

Reason: BASED ON PROFILE

NDA 204,026

Pomalyst (pomalidomide) capsules
1mg, 2mg, 3mg, 4mg

Celgene Corporation

William M. Adams
Review Branch II
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment

For the Division of Hematology Products
Office of Hematology and Oncology Products

Table of Contents

CMC Review Data Sheet

1. NDA 204,026

2. REVIEW #2

3. REVIEW DATE: 15 Jan 2013

4. REVIEWER: William Adams

5. PREVIOUS DOCUMENTS:

N-000	Initial submission	10 Apr 2012
N-001	Request for proprietary name	12 Apr 2012
N-002	Additional (b) (4) DP stability data	11 May 2012
N-003	Additional DP batch analysis data	31 May 2012
N-008	Response to IR-Micro 08/03/12 email	24 Aug 2012
N-009	Response to IR-Micro 08/30/12 email	30 Aug 2012
N-012	Proposed new trade name	08 Sep 2012
N-013	Proposed new trade name	19 Sep 2012
N-016	Response to 09/12/12 Biopharm IR letter	29 Oct 2012
N-017	Additional (b) (4) DP stability data	05 Nov 2012
N-018	Updated labeling	08 Nov 2012
N-019	Updated labeling	20 Nov 2012
N-020	Response to 11/09/12 CMC IR letter	26 Nov 2012
	Tcon with applicant with email response to follow by 12/12/12 and NDA amendments to follow ASAP	10 Dec 2012
	Tcon with applicant with email response to follow by 01/11/13 and NDA amendment submitted the same day	10 Jan 2013

6. SUBMISSION(S) BEING REVIEWED:

---	Email responses to 12/10/12 Tcon	12 Dec 2012
N-021	Response to 11/21/12 Biopharm IR letter	03 Dec 2012
N-023	Responses to 12/10/12 Tcon	14 Dec 2012
N-024	Follow-up to Tcon Question 6 & updated bottle labels	17 Dec 2012
N-030	Response to 01/10/13 Tcon	14 Jan 2013

7. NAME & ADDRESS OF APPLICANT:

Name: Celgene Corporation

Address: 86 Morris Avenue
Summit, NJ 07901

CMC Review Data Sheet

Representative:	Paul McImulty, Director – Regulatory Affairs 400 Connell Drive, Suite 7000 Berkley Heights, NJ 07922
Telephone:	(908) 219-0743

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Pomalyst
b) Non-Proprietary Name (USAN): Pomalidomide Capsule
c) Code Name/# (ONDQA only): CC-4047
d) Chem. Type/Submission Priority (ONDQA only):

- **Chem. Type:** 1
- **Submission Priority:** S

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

10. PHARMACOL. CATEGORY: Immunodulatory agent with antiangiogenic and antineoplastic properties

11. DOSAGE FORM: Hard Gelatin Capsule

12. STRENGTH/POTENCY: 1mg, 2mg, 3mg, 4mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __√__ **Rx** ___ **OTC**

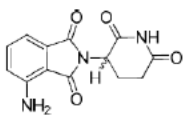
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__√__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Molecular Formula $C_{13}H_{11}N_3O_4$
Molecular Weight 273.24 amu
Molecular Structure



CMC Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. Supporting DMFs: Acceptable in CMC Review 01

B. Other Supporting Documents: See CMC Review 01

18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	SUBJECT	DATE FORWARDED	REVIEWER	STATUS
EES	GMP for CMC sites	04/17/12		Pending OC conclusion
Biopharm	Dissolution Criterion	---	T.M.Chen	Acceptable 12/14/12
Microbiology	Microbial limits	---	S.Donald	Acceptable 09/06/12
Methods Validation	Methods Evaluation	06/11/12		Pending
PharmTox	Impurity criteria		B.Gehrke	Acceptable 12/12/12
DMEPA	Trade name			Acceptable 12/07/12

The CMC Review for NDA 204,026

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application recommended for Approval pending an overall conclusion from the office of compliance.

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

None

II. Summary of CMC Assessments

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

Drug Substance
Pomalidomide is a racemic mixture of a freebase having a single asymmetric carbon. Bulk material is a (b) (4). Molecular structure was established by elemental analysis, NMR spectroscopy, mass spectrometry, single crystal x-ray crystallography and IR spectroscopy.

Manufacturing is performed at two sites in (b) (4) with contract labs (b) (4) for (b) (4) and in (b) (4) for (b) (4) All sites have been found to meet current GMP requirements.

Manufacturing is by a (b) (4) The process consists of a (b) (4). Bulk material is packaged in (b) (4) The manufacturing process and in-process controls are described in sufficient detail. Adequate acceptance specifications are provided for starting materials, solvents and reagents. Product development addresses (b) (4) procedures and studies have established normal operating ranges for the manufacturing process operating parameters.

The release specification addresses appearance, identity, assay, related substances, (b) (4) water content, residue on ignition, heavy metals, and particle size. The analytical methods are described in sufficient detail and validated for the intended use. The proposed criteria are justified by batch analysis data and/or by reference to appropriate ICH guidances.

Reference standards are developed and characterized for drug substance and the primary impurity (b) (4)

Batch analysis data is provided for commercial-scale batches made at both proposed commercial sites by the proposed commercial process. Data is also provided for multiple batches of investigational materials. The expected impurities (b) (4) Materials from both manufacturing sites made by the commercial process have been used in clinical studies.

Stability data is provided from registration studies on batches made by the commercial process at each commercial site; from supportive studies on investigational materials; and from forced degradation and stress studies. The commitments and protocols for the registration studies and post approval studies are adequate. Based on the submitted data and commitments from the applicant, an initial retest period of (b) (4) with storage at USP controlled room temperature is recommended.

Drug Product

Commercial drug product is an immediate release hard gelatin capsules in 1mg, 2mg, 3mg and 4mg strengths. Capsules are color coded, and imprinted with drug name and strength. The market packages are 21-count and 100-count HDPE bottles with a (b) (4) child resistant closure and a tamper evident seal.

Manufacturing is in (b) (4) (b) (4) with a contract packager (b) (4) and stability testing in (b) (4) All except the site in (b) (4) have been found to meet current GMP requirements. A conclusion for this site is pending.

Product development information addressed manufacturability, product stability, drug release profiles, and capsule colorants.

Manufacturing is by a (b) (4) (b) (4) 1mg/2mg and 3mg/4mg strength capsules are obtained from (b) (4) Filled capsules are packaged into bottles for distribution or into a bulk package (b) (4) Process parameters and in-process controls for the manufacture are described in sufficient detail. Excipients meet monograph requirements. No excipient is novel or of human or animal origin. (b) (4) Acceptance specifications for the packaging components are adequate for the intended purpose. Executed batch records for 1mg, 2mg, 3mg, 4mg strength capsules for drug product (b) (4) are provided.

The release specification addresses appearance, identity, assay, related substances, content uniformity and dissolution. The analytical methods are described in sufficient detail and have been validated for their intended use. The proposed criteria are justified by batch analysis data and by reference to ICH guidances. The proposed dissolution criterion has been accepted by the biopharmaceutics reviewer.

Batch analysis data is provided for capsules of each strength; not all combinations of drug product manufacturing sites and drug substance suppliers are represented. Based on low impurity levels in both drug substance and drug product lots, and clinical experience for both drug substance suppliers, this is accepted to address within process variability.

The stability commitments and protocols for the NDA registration studies, and for post approval studies are acceptable. Stability study data is provided from capsules in bulk containers; from primary studies for each capsule manufacturing site, and from supportive studies on investigational batches. Study data does not address all combinations of drug substance and drug product sites, but is accepted based on very small observed chnges in the submitted studies. A maximum holding time of (b) (4) with storage at USP controlled room temperature is recommended for bulk capsules. An initial expiry period of 18 months is recommended for capsules in the commercial packaging systems with storage at USP controlled room temperature.

Draft bottle labels, package insert and patient medication guide are provided.

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

Pomalyst in combination with dexamethasone is indicated for patients with relapsed and refractory multiple myelomas having received prior treatment. The recommended dose of pomalidomide is 4 mg per day to be taken with water on days 1-21 of 28 day cycles until disease progression. Dosing (b) (4) without food. Patients should not break, chew or open capsules. Patients should be dispensed no more than a 28 day supply. (b) (4)

C. Basis for Approvability or Not-Approval Recommendation

Except for an overall conclusion form the office of compliance, complete and acceptable CMC information has been submitted in the application.

III. Administrative

A. Reviewer's Signature: (See appended electronic signature page)

William M. Adams
CMC Reviewer/Branch II/DNDQA I/ONDQA

B. Endorsement Block:

Nallaperum Chidambaram, Ph.D.
Chief/Branch II/DNDQA I/ONDQA

C. CC Block: entered electronically in DFS

OHOP/DHP/RPM/A.Baird

Executive Summary Section

DNDQA I/PMQ/J.Martin
DNDQA I/CMC Lead/J.Brown

20 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

---

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

/s/

WILLIAM M ADAMS
01/15/2013

NALLAPERUM CHIDAMBARAM
01/15/2013
I concur.

NDA 204,026

Pomalyst (pomalidomide) capsules
1mg, 2mg, 3mg, 4mg

Celgene Corporation

William M. Adams
Review Branch II
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment

For the Division of Hematology Products
Office of Hematology and Oncology Products

Table of Contents

CMC Review Data Sheet

1. NDA 204,026

2. REVIEW #1

3. REVIEW DATE: 14 Dec 2012

4. REVIEWER: William Adams

5. PREVIOUS DOCUMENTS: None

6. SUBMISSION(S) BEING REVIEWED:

N-000	Initial submission	10 Apr 2012
N-001	Request for proprietary name	12 Apr 2012
N-002	Additional (b) (4) DP stability data	11 May 2012
N-003	Additional DP batch analysis data	31 May 2012
N-008	Response to IR-Micro 08/03/12 email	24 Aug 2012
N-009	Response to IR-Micro 08/30/12 email	30 Aug 2012
N-012	Proposed new trade name	08 Sep 2012
N-013	Proposed new trade name	19 Sep 2012
N-016	Response to 09/12/12 Biopharm IR letter	29 Oct 2012
N-017	Additional (b) (4) DP stability data	05 Nov 2012
N-018	Updated labeling	08 Nov 2012
N-019	Updated labeling	20 Nov 2012
N-020	Response to 11/09/12 CMC IR letter	26 Nov 2012
	Tcon with applicant with email response to follow by 12/12/12 and NDA amendments to follow ASAP	10 Dec 2012

7. NAME & ADDRESS OF APPLICANT:

Name:	Celgene Corporation
Address:	86 Morris Avenue Summit, NJ 07901
Representative:	Paul McImulty, Director – Regulatory Affairs 400 Connell Drive, Suite 7000 Berkley Heights, NJ 07922
Telephone:	(908) 219-0743

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Pomalyst
b) Non-Proprietary Name (USAN): Pomalidomide Capsule
c) Code Name/# (ONDQA only): CC-4047

d) Chem. Type/Submission Priority (ONDQA only):

- **Chem. Type:** 1
- **Submission Priority:** S

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

10. PHARMACOL. CATEGORY: Immunodulatory agent with antiangiogenic and antineoplastic properties

11. DOSAGE FORM: Hard Gelatin Capsule

12. STRENGTH/POTENCY: 1mg, 2mg, 3mg, 4mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: √ Rx ___OTC

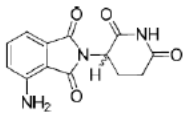
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__√__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Molecular Formula $C_{13}H_{11}N_3O_4$
Molecular Weight 273.24 amu
Molecular Structure



17. RELATED/SUPPORTING DOCUMENTS:

A. Supporting DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS[3]
(b) (4)	III	(b) (4)	(b) (4)	4			
	III			4			

(b) (4)		(b) (4)	(b) (4)				
	III			4			
	III			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)
[3] Include reference to location in most recent CMC review

B. Other Supporting Documents:

Doc #	OWNER	ITEM REFERENCED	STATUS	DATE REVIEW COMPLETED	COMMENTS
IND 66188	Celgene Corp.	CC-4047	Active		

18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	SUBJECT	DATE FORWARDED	REVIEWER	STATUS
EES	**GMP for CMC sites**	**04/17/12**		**Pending**
Biopharm	**Dissolution Criterion**	---	**T.M.Chen**	**Pending**
Methods Validation	**Methods Evalaution**	**06/11/12**		**Pending**

The CMC Review for NDA 204,026

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is Not Adequate with regard to chemistry, manufacturing and control (CMC) information in that additional information is to be submitted, and an overall OC conclusion in EES is still pending. Until the technical issues are resolved, it is recommended that a Complete Response action be taken.

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

None

II. Summary of CMC Assessments

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

Drug Substance

Pomalidomide is a racemic mixture of a freebase having a single asymmetric carbon. Bulk material is (b) (4) Molecular structure was established by elemental analysis, NMR spectroscopy, mass spectrometry, single crystal x-ray crystallography and IR spectroscopy.

Bulk drug is to be manufactured at two sites in (b) (4) (b) (4) There will be contract labs in (b) (4) for release testing and in (b) (4) for stability testing. All sites have been established to meet current GMP requirements.

The drug substance is manufactured by a (b) (4) The process consists of the (b) (4) Bulk packaging is (b) (4) The manufacturing process and in-process controls are described in sufficient detail. Adequate acceptance specifications are provided for starting materials, solvents and reagents. Product development addresses (b) (4) and studies have established normal operating ranges (NORs) for the manufacturing process operating parameters. Proposed proven acceptable ranges (PARs) for process parameters were rejected due to insufficient supporting information. A design space for process parameters was not proposed.

The release specification addresses appearance, identity, assay, related substances, (b) (4) , water content, residue on ignition, heavy metals, and particle size. Except for minor revisions, the analytical methods are described in sufficient detail and validated for the intended use. The proposed criteria are justified by batch analysis data and by reference to appropriate ICH guidances. Reference standards are developed and characterized for drug substance and the primary impurity (b) (4)

Batch analysis data is provided for commercial-scale batches of material made at the commercial sites by the commercial process. Data is also provided for batches of investigational material. The expected impurities (b) (4) Total impurities are reported (b) (4) unknown impurity for material from (b) (4). The application indicates that there is no clinical experience with material from (b) (4). The applicant has committed to provide additional information establishing the comparability for safety and quality of materials from each manufacturing site. This information is pending.

Stability data is provided from registration studies on batches made by the commercial process at each commercial site; from supportive studies on investigational material; and from forced degradation and stress studies. The commitments and protocols for the registration studies and post approval studies are adequate, except for minor revisions. Based on submitted data and the commitment from the applicant, an initial retest period of (b) (4) with storage at USP controlled room temperature is recommended.

Drug Product

The commercial drug product is in 1mg, 2mg, 3mg and 4mg strengths based on the freebase. The dosage form is a color codes immediate release, opaque hard gelatin capsule imprinted with drug name and strength. Capsules are packaged in 21-count and 100-count HDPE bottles with a (b) (4) child resistant closure and a tamper evident seal.

Drug product is to be manufactured in Switzerland (Celgene Sarl) and (b) (4) with a contract packager in (b) (4) Stability testing will be performed in New Jersey. All sites, except (b) (4), have been established to meet current GMP requirements. A conclusion for the (b) (4) site is pending.

Drug product development information addressed manufacturability, product stability, drug release profiles, and capsule colorants.

The drug product is manufacture is by (b) (4) 1mg/2mg and 3mg/4mg strength capsules are obtained from (b) (4) Filled capsules are packaged into bottles for distribution or into a bulk package (b) (4) Process parameters and in-process controls for the manufacture are described in sufficient detail. Excipients meet monograph requirements. No excipient is novel or of human or animal origin. (b) (4) Acceptance specifications for commercial packaging components are adequate

for the intended purpose. Executed batch records for 1mg, 2mg, 3mg, 4mg strength capsules made at (b) (4) using drug substance from (b) (4) are provided.

The release specification addresses appearance, identity, assay, related substances, content uniformity and dissolution. The analytical methods are described in sufficient detail and have been validated for their intended use. The proposed criteria are justified by batch analysis data and by reference to ICH guidances. The applicant has agreed to a revised criterion for dissolution proposed by the biopharmaceutics reviewer.

Batch analysis data is provided for capsules of each strength made at Celgene Sarl with drug substance from (b) (4) and for capsules of each strength made at (b) (4) with drug substance from (b) (4) Data on capsules from (b) (4) show (b) (4) impurities and capsules from Celgene Sarl show (b) (4) unknown impurity. The applicant has committed to provide data establishing comparability of materials for quality and safety; and to address the relationship of (b) (4) the observed drug release profiles. The information is pending.

The stability commitments and protocols for the registration batches and the post approval studies has been tentatively accepted. The applicant has agreed to revise the stability protocols and the submission is pending. The applicant has agree to provide stability data on the capsules in bulk packaging. Stability information consists of data from primary studies on Celgene Sarl capsules made with drug substance from (b) (4) capsules made with drug substance from (b) (4); and supportive studies on investigational batches. Based on commitments from the applicant and the submitted stability study data, it was agree that an initial expiry period of 18 months with storage at USP controlled room temperature is supported.

Draft bottle labels, package insert and patient medication guide are provided. The CMC information is acceptable except for the need to present the storage condition as a range instead of a single temperature value.

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

Pomalyst in combination with dexamethasone is indicated for patients with relapsed and refractory multiple myelomas having received prior treatement. The recommended dose of pomalidomide is 4 mg per day to be taken with water on days 1-21 of 28 day cycles until disease progression. Dosing (b) (4) without food. Patients should not break, chew or open capsules. Patients should be dispensed no more than a 28 day supply. (b) (4)

C. Basis for Approvability or Not-Approval Recommendation

In a Tcon on 10 Dec 2012, CMC issues regarding the release specifications and stability information for drug substance and drug product; and biopharmaceutics issues regarding the dissolution criterion and the effect of (b) (4) on the dissolution profile were discussed. The applicant agreed to provide additional information by 12 Dec 2012 with follow-up of revised NDA sections in electronic format as soon as available. In addition, an overall OC conclusion

has not been previded in EES. A conclusion regarding approvability for the application is withheld pending resolution of these issues.

III. Administrative

A. Reviewer's Signature: (See appended electronic signature page)

William M. Adams
CMC Reviewer/Branch II/DNDQA I/ONDQA

B. Endorsement Block:

Nallaperum Chidambaram, Ph.D.
Chief/Branch II/DNDQA I/ONDQA

C. CC Block: entered electronically in DFS

OHOP/DHP/RPM/A.Baird
DNDQA I/PMQ/J.Martin
DNDQA I/CMC Lead/J.Brown

125 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

---

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

/s/

WILLIAM M ADAMS
12/14/2012

NALLAPERUM CHIDAMBARAM
12/14/2012

The following issues are pending:
1. Technical issues
2. Labeling
3.Overall acceptable recommendation from the Office of Compliance.

I concur.

PRODUCT QUALITY (Small Molecule)
FILING REVIEW FOR NDA or Supplement (ONDQA)

NDA Number:	Supplement Number and Type:	Established/Proper Name:
204026	Original NDA	Pomalidomide Capsules
Applicant:	**Letter Date:**	**Stamp Date:**
Celgene Corporation	10-Apr-2012	10-Apr-2012

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies. On **initial** overview of the NDA application for filing:

A. GENERAL				
	Parameter	**Yes**	**No**	**Comment**
1.	Is the CMC section organized adequately?	X		
2.	Is the CMC section indexed and paginated (including all PDF files) adequately?	X		
3.	Are all the pages in the CMC section legible?	X		
4.	Has all information requested during the IND phase, and at the pre-NDA meetings been included?	X		

B. FACILITIES*				
	PARAMETER	**YES**	**NO**	**COMMENT**
5.	Is a single, comprehensive list of all involved facilities available in one location in the application?	X		
6.	For a naturally-derived API only, are the facilities responsible for critical intermediate or crude API manufacturing, or performing upstream steps, specified in the application? If not, has a justification been provided for this omission? **This question is not applicable for synthesized API.**			NA
7.	Are drug substance manufacturing sites identified on FDA Form 356h or associated continuation sheet? For each site, does the application list: • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable)	X		

B. FACILITIES*				
	PARAMETER	**YES**	**NO**	**COMMENT**
8.	Are drug product manufacturing sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list: • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable)	X		
9.	Are additional manufacturing, packaging and control/testing laboratory sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list: • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable)	X		
10.	Is a statement provided that all facilities are ready for GMP inspection at the time of submission?	X		

* If any information regarding the facilities is omitted, this should be addressed ASAP with the applicant and can be a *potential* filing issue or a *potential* review issue.

C. ENVIRONMENTAL ASSESMENT				
	Parameter	**Yes**	**No**	**Comment**
11.	Has an environmental assessment report or categorical exclusion been provided?	X		

D. DRUG SUBSTANCE/ACTIVE PHARMACEUTICAL INGREDIENT (DS/API)				
	Parameter	**Yes**	**No**	**Comment**
12.	Does the section contain a description of the DS manufacturing process?	X		
13.	Does the section contain identification and controls of critical steps and intermediates of the DS?	X		
14.	Does the section contain information regarding the characterization of the DS?	X		
15.	Does the section contain controls for the DS?	X		
16.	Has stability data and analysis been provided for the drug substance?	X		
17.	Does the application contain Quality by Design (QbD) information regarding the DS?			Under evaluation by QbD Liaison
18.	Does the application contain Process Analytical Technology (PAT) information regarding the DS?		X	
E. drug product (dp)				
	Parameter	**Yes**	**No**	**Comment**
19.	Is there a description of manufacturing process and methods for DP production through finishing, including formulation, filling, labeling and packaging?	X		
20.	Does the section contain identification and controls of critical steps and intermediates of the DP, including analytical procedures and method validation reports for assay and related substances if applicable?	X		
21.	Is there a batch production record and a proposed master batch record?	X		
22.	Has an investigational formulations section been provided? Is there adequate linkage between the investigational product and the proposed marketed product?	X		
23.	Have any biowaivers been requested?		X	
24.	Does the section contain description of to-be-marketed container/closure system and presentations)?	X		
25.	Does the section contain controls of the final drug product?	X		
26.	Has stability data and analysis been provided to support the requested expiration date?	X		Expiry will be determined by primary reviewers in ONDQA
27.	Does the application contain Quality by Design (QbD) information regarding the DP?			Under review by QbD Liaison
28.	Does the application contain Process Analytical Technology (PAT) information regarding the DP?		X	

F. METHODS VALIDATION (MV)				
	Parameter	Yes	No	Comment
29.	Is there a methods validation package?	X		

G. MICROBIOLOGY				
	Parameter	Yes	No	Comment
30.	If appropriate, is a separate microbiological section included assuring sterility of the drug product?		X	Microbial Limits Testing

H. MASTER FILES (DMF/MAF)				
	Parameter	Yes	No	Comment
31.	Is information for critical DMF references (i.e., for drug substance and important packaging components for non-solid-oral drug products) complete?	X		
I. Labeling				
	Parameter	Yes	No	Comment
32.	Has the draft package insert been provided?	X		
33.	Have the immediate container and carton labels been provided?	X		

J. FILING CONCLUSION				
	Parameter	**Yes**	**No**	**Comment**
34.	**IS THE PRODUCT QUALITY SECTION OF THE APPLICATION FILEABLE?**	X		
35.	If the NDA is not fileable from the product quality perspective, state the reasons and provide **filing** comments to be sent to the Applicant.			N.A.
36.	Are there any **potential review** issues to be forwarded to the Applicant for the 74-day letter?		X	

{See appended electronic signature page}

Janice Brown — Date: 01-Jun-2012
Pharmaceutical Assessment Lead or CMC Lead / CMC Reviewer
Division of Pre-Marketing Assessment 1
Office of New Drug Quality Assessment

{See appended electronic signature page}

Sarah Pope Miksinski, Ph.D. — Date: 01-Jun-2012
Chief, Branch 2
Division of Pre-Marketing Assessment 1
Office of New Drug Quality Assessment

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

/s/

JANICE T BROWN
06/09/2012

SARAH P MIKSINSKI
06/11/2012