

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205582Orig1s000

CHEMISTRY REVIEW(S)

NDA 205582

Decitabine for Injection, 50 mg

Sun Pharma Global FZE

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**

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CMC Review Data Sheet

CMC Review Data Sheet

1. **NDA 205582**
2. **REVIEW #1**
3. **REVIEW DATE:** 11 Dec 2013
4. **REVIEWER:** William Adams
5. **PREVIOUS DOCUMENTS:** None
6. **SUBMISSION(S) BEING REVIEWED:**

<i>eCTD Sequence</i>	<i>Submitted</i>	<i>Received</i>	<i>Description</i>
S-000	03/27/13	03/27/13	Initial Submission
S-005	10/11/13	10/11/13	CMC Amendment
S-007	11/22/13	11/22/13	Labeling Amendment
S-008	12/03/13	12/03/13	Labeling Amendment

7. **NAME & ADDRESS OF APPLICANT:**

Name Sun Pharma Global FZE
 Address Office 43, Block Y SAIF, P.O. Box 122304
 Sharjah, UAE
 Representative Karin A. Kook, Ph.D., Salamandra LLC
 One Bethesda Center, 4800 Hampden Lane, Suite 900
 Bethesda, MD 20814-2998
 Email kkook@salamandra.net
 Telephone 301-652-6110

8. **DRUG PRODUCT NAME/CODE/TYPE:**

- a) **Proprietary Name:** None
- b) **Non-Proprietary Name (USAN):** Decitabine for Injection
- c) **Code Name/# (ONDQA only):** DCB
- d) **Chem. Type/Submission Priority (ONDQA only):**
 - **Chem. Type:** 3
 - **Submission Priority:** Standard

9. **LEGAL BASIS FOR SUBMISSION:** 505(b)(2)

CMC Review Data Sheet

- 10. **PHARMACOL. CATEGORY:** Nucleoside metabolic inhibitor for the treatment of patients with myelodysplastic syndromes (MDS)
- 11. **DOSAGE FORM:** Lyophilized Powder for Injection
- 12. **STRENGTH/POTENCY:** 50 mg/vial
- 13. **ROUTE OF ADMINISTRATION:** IV infusion
- 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 $C_8H_{12}N_4O_4$
Molecular Weight (b) (4)
Molecular Structure (b) (4)

- 17. **RELATED/SUPPORTING DOCUMENTS:**

A. Supporting DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	REVIEW COMPLETED	COMMENTS ³
26256	II	Sun Pharmaceutical Industries, Ltd	Bulk drug substance	1	adequate		
(b) (4)	III	(b) (4)	(b) (4)	4			
(b) (4)	III	(b) (4)	(b) (4)	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

CMC Review Data Sheet

- 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 114119	Sun Pharmaceutical Industries, Ltd.	Decitabine for Injection, 50 mg/vial	Active		

18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	SUBJECT	DATE FORWARDED	REVIEWER	STATUS
EES	GMP for CMC sites	04/17/12	OC	Adequate 05/01/13
Microbiology	Sterility Assurance	04/15/13	N.Sweeney	Adequate 11/14/13

Executive Summary Section

The CMC Review for NDA 205,582

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is recommended for APPROVAL in that adequate chemistry, manufacturing and control (CMC) information is provided in DMF 26256 and in this application.

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)

This is a 505(b)(2) application based on the Eisai's NDA 21790 for Dacogen®, Decitabine for Injection, 50 mg/vial. The Reference Product is a sterile, lyophilized powder containing Decitabine and the ingredients of a (b) (4) phosphate (b) (4) in a single-use glass vial which is to be reconstituted with sterile Water for Injection, USP to a concentration of 5 mg/mL Decitabine then admixed with 0.9% Sodium Chloride Injection, USP; 5% Dextrose Injection, USP; or Lactated Ringer's Injection, USP to a concentration of 0.1-1.0 mg/mL for intravenous infusion.

The proposed product is in two parts. The Drug Product is a lyophilized drug substance in a single-use glass vial. The Diluent is an aqueous (b) (4) solution in a single-use glass vial. The vials are presented together in a combi-pack cardboard carton with appropriate labels and labeling. Drug Product is to be reconstituted with Diluent to obtain a 5 mg/mL solution of Decitabine which is to be then admixed as with Dacogen® for intravenous infusion. Reconstituted solutions of the proposed product and Dacogen® are shown to be qualitatively and quantitatively the same.

Complete CMC information on Drug Substance is provided in Sun Pharmaceutical Industries Ltd's type II DMF 26256. The application includes a synopsis of key CMC information on drug substance, and complete CMC information on Drug Product and Diluent. The applicant's claim for a categorical exclusion from the environmental assessment requirement for Drug Product and Diluent is acceptable. Acceptable labels and labeling are provided for Drug Product and Diluent.

DRUG PRODUCT

Executive Summary Section

The commercial presentation is a sterile, lyophilized powder composed of drug substance and no excipients in a glass vial with elastomeric stopper and baby blue flipoff overseal in a combi-pack with Diluent.

A product development report addresses formulation, manufacturing operations, process parameters (including solution hold times), in-process controls, packaging components, container/closure integrity, and stability of the reconstituted solution and admixture solutions. Decitabine in solution is shown to be very sensitive to heat, light, acid hydrolysis, base hydrolysis and oxidation.

Manufacture, control and packaging are performed by Sun Pharmaceutical Industries Ltd at their Halol, Gujarat, India site with biological testing of packaging components by Sun Pharmaceutical Industries Ltd at their Tandajja, Gujarat, India facility. The sites have been found to meet cGMP expectations. Manufacture is by (b) (4). The manufacturing procedure, process parameters, and in-process controls are described in sufficient detail. Provided are an executed batch record for 1 exhibit batch manufactured at (b) (4) commercial-scale, and a copy of the proposed manufacturing record for the commercial-scale process. Studies qualifying the process equipment and parameters are provided. The specifications for Decitabine, in-house; and process materials ((b) (4)) are acceptable.

The proposed release specification is adequate in that it addresses identity; assay; organic and inorganic impurities; (b) (4) water content; weight variation; and USP <1> requirements. The proposed analytical methods are described in sufficient detail and validated for their intended use. Reference standards for specified organic impurities are addressed in DMF 26256. The proposed acceptance criteria are justified by process capability; ICH Q3C safety limits; USP expectations; and safety studies on specified organic impurities. Batch analysis data from 3 exhibit batches is provided. Each batch meets the proposed specification.

The applicant has committed to re-evaluate the proposed criteria for (b) (4) in drug product based on commercial batch analysis data. A formal PMR or PMC was not submitted.

The proposed commercial packaging system (b) (4). Specifications for the proposed packaging components are acceptable.

Data from primary studies and a forced degradation study using the 3 exhibit batches is sufficient to support an initial expiry period of 24 months with storage at USP controlled room temperature in the proposed packaging system and combi-pack. An acceptable post approval stability protocol and commitment are provided.

Executive Summary Section

DILUENT

The commercial presentation is a sterile, aqueous, (b) (4) phosphat (b) (4) in a glass vial with elastomeric stopper and transparent flipoff overseal in a combi-pack with Drug Product.

A product development report addresses formulation, manufacturing process parameters, and equipment compatibility. The (b) (4) solution is shown to be chemically stable.

Manufacture, control and packaging are performed at the same site as for Drug Product.

Manufacture is by (b) (4)

(b) (4) The manufacturing procedure, process parameters, and in-process controls are described in sufficient detail. Provided are an executed batch record for 1 exhibit batch manufactured at (b) (4) commercial-scale, and a copy of the proposed manufacturing record for the commercial-scale process. Studies qualifying the process equipment and parameters are provided. Specifications for the excipients (monobasic potassium phosphate, NF; sodium hydroxide, NF; and water for injection, USP) are acceptable.

The proposed release specification is adequate in that it addresses identity; pH; (b) (4); fill volume; and USP <1> requirements. The proposed analytical methods are described in sufficient detail; validation was not needed. No reference standards are used. The proposed acceptance criteria are justified by manufacturing experience, and USP expectations. Batch analysis data from 3 exhibit batches manufactured at (b) (4) commercial scale is provided. Each batch meets the proposed specification.

The proposed commercial packaging system is a single-use, 10cc clear tubular glass vial, bromobutyl elastomeric closure and transparent flipoff aluminium overseal. Specifications for the proposed packaging components are acceptable.

Data from primary studies and a forced degradation study using the 3 exhibit batches is sufficient to support an initial expiry period of 24 months with storage at USP controlled room temperature in the proposed packaging system and combi-pack. An acceptable post approval protocol and commitment are provided.

DRUG SUBSTANCE

Complete and acceptable CMC information regarding bulk drug substance is provided in type II DMF 26256 which is addressed in a separate review.

Decitabine is a white powder which is soluble in dimethylsulfoxide and in water; is hygroscopic; is labile to hydrolysis; and is cytotoxic.

Manufacture and control are performed by Sun Pharmaceutical Industries Ltd at their Ahmednagar, Maharashtra, India site. The site has been found to meet cGMP expectations. Manufacturing procedure, process parameters, in-process controls, intermediate specifications, and reagent specifications are acceptable and are described in sufficient detail.

Executive Summary Section

The proposed release specification is adequate in that it addresses identity; assay; impurities; residual solvents; and bioburden. The proposed analytical methods are described in sufficient detail and validated for the intended use. The proposed acceptance criteria are sufficiently justified. Batch analysis data is provided for the lots used to manufacture the drug product exhibit batches.

The packaging system proposed for storage and shipment is described in sufficient detail and the proposed component specifications are acceptable.

Data from primary stability studies and a forced degradation study are sufficient to support the proposed retest period of (b) (4) months with storage at 2-8°C in the proposed storage container. An acceptable post approval stability protocol and commitment are provided.

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

Decitabine for Injection is a cytotoxic drug which is intended to be reconstituted with Decitabine for Injection Diluent to a concentration of 5 mg/mL, then immediately admixed with 0.9% Sodium Chloride Injection, USP; 5% Dextrose Injection, USP; or Lactated Ringer's Injection, USP to a concentration of 0.1-1.0%. This solution is to be administered by intravenous infusion. The admixture solution may be stored at room temperature for up to 15 minutes or at 2-8°C for up to 7 hours before administration.

C. Basis for Approvability or Not-Approval Recommendation

CMC information on Drug Substance provided in type II DMF 25256; and on Drug Product and Diluent provided in this application is complete and described in sufficient detail. All deficiencies have been addressed, and acceptable labels and labeling are provided.

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

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

B. Endorsement Block:

Ali al Hakim, Ph.D.
Chief/Branch II/DNDQA I/ONDQA

C. CC Block: entered electronically in DFS

DHP/RPM/L.Akinsanya
DNDQA I/PMQ/J.Martin
DNDQA I/CMC Lead/J.Brown

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/s/

WILLIAM M ADAMS
12/12/2013

ALI H AL HAKIM
12/12/2013

**Initial Quality Assessment
Division of New Drug Quality Assessment I
Branch II**

OND Division: Division of Hematology Products
 NDA: 205582
 Applicant: Sun Pharma Global FZE
 Authorized U.S. Agent: Karin A. Kook, Ph.D., Salamandra, LLC
 Stamp Date: 27-Mar-2013
 PDUFA Date: 07-Sep-2013
 Proprietary (Brand) Name of Drug Product: N.A.
 Established Name: Decitabine for Injection (50 mg/vial) and Diluent for Decitabine for Injection (50 mg/vial)
 Dosage Form(s): Injection, Powder, for Solution
 Strength(s): 50 mg/Vial
 Route of Administration: Intravenous
 Proposed Indication(s): Indicated for treatment of patients with MDS including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.
 Pharmacologic Class: Antineoplastic Agent
 CMC Lead: Janice Brown, Branch II/DNDQA1/ONDQA
 Chief, Branch II: Ali Al Hakim, DNDQA1/ONDQA

	Yes	No
ONDQA Fileability:	X	<input type="checkbox"/>
Comments for 74-Day Letter	<input type="checkbox"/>	X

CONSULTS/ CMC RELATED REVIEWS

Consult	Comment
Biopharmaceutics	Elsbeth Chikhale
CDRH	Not Applicable
EA	Categorical exclusion requested
EES	Refer to attachment 1 for a list of manufacturing sites submitted in EES
Methods Validation	Not required per IQP 5105
Microbiology	Neal Sweeney
Pharm/Tox	To be determined by Primary Reviewer

SUMMARY

This 505(b)(2) application relies on the FDA's finding of safety and effectiveness for the listed drug, Dacogen (decitabine) for Injection marketed by Eisai Inc. under the approved NDA # 21790. Decitabine, an analogue of the natural nucleoside 2'-deoxycytidine, is approved for treatment of patients with myelodysplastic syndrome (MDS). Decitabine for Injection, like Dacogen®, is intended for administration by injection as an intravenous infusion over either 1 or 3 hours. The proposed indications and dosing instructions for Sun's Decitabine for Injection are identical to those of the currently approved product. There are two approved regimens for Dacogen administration:

- 15 mg/m², given as a continuous infusion over 3 hours every 8 hours for 3 days; the cycle is to be repeated every 6 weeks
- 20 mg/m², given as a continuous infusion over 1 hour daily for 5 days; the cycle is to be repeated every 4 weeks

No clinical safety, efficacy or clinical pharmacology studies were submitted in this NDA. A repeat dose toxicity study was performed to support the level of two impurities ((b) (4) and (b) (4)) that exceed the ICH qualification threshold after the drug product has been reconstituted and further diluted in 0.9 % sodium chloride injection, 5% dextrose injection, or Lactated Ringer's solution to produce the admixture.

Decitabine is pyrimidine nucleoside analog. It differs from natural nucleoside deoxycytidine by the presence of nitrogen at position 5(*) of cytosine ring (see figure 1). The substitution at 5-position prevents methylation and consequently affects the DNA transcriptional activity which results in anti-neoplastic activity.

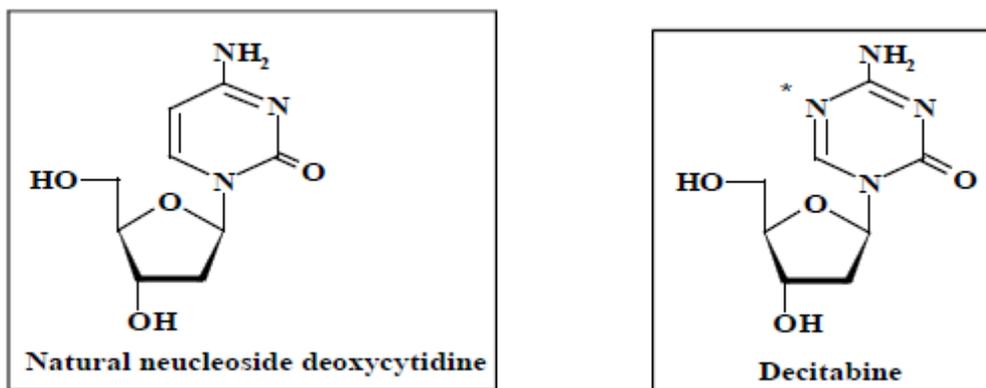


Figure 1: Comparison of the natural nucleoside deoxycytidine with decitabine.

The applicant's proposed Decitabine for Injection will be available as a combination pack that includes a product vial (containing only decitabine) and diluent vial (containing (b) (4) and water). This is a new formulation of Decitabine for Injection, when reconstituted with the accompanying diluent will be identical in composition to the listed drug, Dacogen. The drug product vial contains only decitabine without any (b) (4). The diluent supplied with the drug product contains monobasic potassium phosphate and sodium hydroxide. Upon reconstitution

with the diluent the drug product is identical to the listed drug. A comparison table of decitabine for injection from the listed drug (Eisai) and Sun Pharma is summarized in table 1 below.

Table 1: Comparative Presentations/Compositions: Dacogen® versus Sun's Product

	Dacogen® (decitabine for injection) RLD (NDA 021790)	Decitabine for Injection (Sun)
Lyophilized Drug Vial (20-mL Glass):		
Decitabine	50 mg	50 mg
Monobasic potassium phosphate, NF	68 mg	--
Sodium hydroxide, NF	11.6 mg	--
Diluent (for Sun product, 10-mL Glass Vial):		
Water for injection, USP	Not supplied; 10 mL of Water for Injection, USP	10 mL
Monobasic potassium phosphate, NF		68 mg
Sodium hydroxide, NF		11.6 mg
Drug + Diluent (Initial Reconstitution¹):		
Decitabine	50 mg	50 mg
Monobasic potassium phosphate, NF	68 mg	68 mg
Sodium hydroxide, NF	11.6 mg	11.6 mg
Sterile Water for Injection	10 mL	10 mL

¹ After initial reconstitution, both Decitabine for Injection and Dacogen® preparations are to be further diluted in intravenous solutions before administration to a patient.

DRUG SUBSTANCE

1. The applicant provided a letter of authorization from Sun Pharmaceuticals allowing the agency to review the confidential information in DMF No. 26256.
2. Decitabine drug substance is manufactured and controlled by:

Sun Pharmaceutical Industries Limited,
 Acme Plaza, Andheri-Kurla Road, Andheri (East),
 Mumbai - 400059, India

3.  (b) (4)

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
05/14/2013

ALI H AL HAKIM
05/14/2013

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

NDA Number:	Supplement Number and Type:	Established/Proper Name:
205582	NA	Decitabine for Injection (50 mg/vial) and Diluent for Decitabine for Injection (50 mg/vial)
Applicant:	Letter Date:	Stamp Date:
Sun Pharma Global FZE.	03/27/2013	03/27/2013

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

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

7.	<p>Are drug substance manufacturing sites identified on FDA Form 356h or associated continuation sheet? For each site, does the application list:</p> <ul style="list-style-type: none"> • 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		
8.	<p>Are drug product manufacturing sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:</p> <ul style="list-style-type: none"> • 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		

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

9.	<p>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:</p> <ul style="list-style-type: none"> • 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		

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

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		Referenced DMF No. 26256
13.	Does the section contain identification and controls of critical steps and intermediates of the DS?	X		Referenced DMF No. 26256
14.	Does the section contain information regarding the characterization of the DS?	X		Referenced DMF No. 26256
15.	Does the section contain controls for the DS?	X		Referenced DMF No. 26256
16.	Has stability data and analysis been provided for the drug substance?	X		Referenced DMF No. 26256
17.	Does the application contain Quality by Design (QbD) information regarding the DS?		X	
18.	Does the application contain Process Analytical Technology (PAT) information regarding the DS?		X	

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

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		
	Does the section contain description of to-be-marketed container/closure system and presentations)?	X		
24.	Does the section contain controls of the final drug product?	X		
25.	Has stability data and analysis been provided to support the requested expiration date?	X		
26.	Does the application contain Quality by Design (QbD) information regarding the DP?	X		See IQA
27.	Does the application contain Process Analytical Technology (PAT) information regarding the DP?		X	

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

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

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

H. MASTER FILES (DMF/MAF)				
	Parameter	Yes	No	Comment
30.	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
31.	Has the draft package insert been provided?	X		
32.	Have the immediate container and carton labels been provided?	X		

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

J. FILING CONCLUSION				
	Parameter	Yes	No	Comment
33.	IS THE PRODUCT QUALITY SECTION OF THE APPLICATION FILEABLE?	X		
34.	If the NDA is not fileable from the product quality perspective, state the reasons and provide filing comments to be sent to the Applicant.			NA
35.	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, Branch II/DNDQA1/ONDQA

14-May-2013

{See appended electronic signature page}

Ali Al-Hakim, Ph.D. /DNDQA1/ONDQA

14-May-2013

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
05/14/2013

ALI H AL HAKIM
05/14/2013