

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205582Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 205582

SUPPL # N/A

HFD # 161

Trade Name Decitabine Injection

Generic Name N/A

Applicant Name Sun Pharma Global

Approval Date, If Known January 27, 2014

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

N/A

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If

the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently

demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

interest provided substantial support for the study?

Investigation #1
!
! YES ! NO
! Explain: ! Explain:

Investigation #2
!
! YES ! NO
! Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

=====
Name of person completing form: Lara Akinsanya, M.S.
Title: Senior Regulatory Health Project Manager
Date: December 27, 2013

Name of Office/Division Director signing form: Edvardas Kaminskas, M.D.
Title: Deputy Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

21 Page(s) of Draft Labeling have 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/

MONSURAT O AKINSANYA
01/23/2014

EDVARDAS KAMINSKAS
01/23/2014

Sun Pharma Global FZE

NDA for Decitabine for Injection, 50 mg/Vial

1.3.3 Debarment Certification-GDEA (Generic Drug Enforcement Act)

Pursuant to Section 306(k)(1) of the Federal Food, Drug and Cosmetic Act, as amended by the Generic Drug Enforcement Act of 1992, Sun Pharma Global FZE hereby certifies that it did not and will not use, in any capacity, the services of any person debarred under subsection (a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this NDA.

W. Kenkare

Mr. Vishwanath Kenkare
Manager,
Sun Pharma Global FZE
Date: March 22, 2013

NDA 205582
Decitabine Injection


Jan 23, 2014

Financial Disclosure Review

Financial Disclosure is not needed for this application because no clinical efficacy or safety data were submitted in this NDA.

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 205582 BLA # N/A	NDA Supplement # N/A BLA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A
Proprietary Name: N/A Established/Proper Name: Decitabine Dosage Form: Injection		Applicant: Sun Pharma Global Agent for Applicant (if applicable): N/A
RPM: Lara Akinsanya		Division: Division of Hematology Products
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(For additional information regarding 505(b)(2)s, please refer to http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/RegulatoryAffairsTeam/ucm027499.htm)</p>	<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)): NDA 21790, Dacogen</p> <p>Provide a brief explanation of how this product is different from the listed drug. Decitabine for Injection is a new formulation and presentation of the approved product, Dacogen®. Decitabine for Injection comes with a diluent that contains monobasic potassium phosphate and sodium hydroxide, while Dacogen contains monobasic potassium phosphate and sodium hydroxide as buffering / pH stabilizing agents in the vial containing the drug product.</p> <p><input type="checkbox"/> This application does not rely upon a listed drug. <input checked="" type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> This application relies on (explain)</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: 1/23/2014</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>	
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>Jan. 27, 2014</u> 	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR	

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 5) lists the documents to be included in the Action Package.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<ul style="list-style-type: none"> Previous actions (<i>specify type and date for each action taken</i>) 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____ 	<input type="checkbox"/> Received
<ul style="list-style-type: none"> Application Characteristics³ 	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input checked="" type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC <input type="checkbox"/> Breakthrough Therapy designation </p> <p> NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies </p> <p> <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request </p> <p>BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies</p> <p>REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required</p> <p>Comments:</p>	
<ul style="list-style-type: none"> BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter) 	<input type="checkbox"/> Yes, dates
<ul style="list-style-type: none"> BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>) 	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Public communications (<i>approvals only</i>) 	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action (by OEP) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ⁴	January 27, 2014
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action and date Approval – January 23, 2014
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	December 3, 2013
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	March 27, 2013
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A

⁴ Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	N/A
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	N/A
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	December 3, 2013
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	N/A N/A
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 01/03/14 <input checked="" type="checkbox"/> DMEPA 12/6/13; 9/19/13 <input type="checkbox"/> DMPP/PLT (DRISK) <input checked="" type="checkbox"/> OPDP (DDMAC) 10/17/13 <input type="checkbox"/> SEALD <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	RPM Filing Review – 5/30/13
<ul style="list-style-type: none"> ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	<input type="checkbox"/> Not a (b)(2) 01/06/14 <input type="checkbox"/> Not a (b)(2) 01/23/14
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>N/A</u> If PeRC review not necessary, explain: <u>This is a 505(b) 2 Application</u> • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications (<i>letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons</i>)	October 18(2); October 10; October 3; October 1; September 17; August 21; June 4; and April 19, 2013
❖ Internal memoranda, telecons, etc.	None
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> 02/07/12
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	None
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/22/14
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 01/06/14
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	12/30/13
• Clinical review(s) (<i>indicate date for each review</i>)	10/17/13 (primary) 5/22/13 (filing)
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input checked="" type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	See memo included dated January 23, 2014
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>)	
• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)	
• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	<input checked="" type="checkbox"/> None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested

⁶ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Clinical Microbiology Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Biostatistics <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Statistical Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Statistical Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> 8/14/13 – co-signed primary review
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 8/8/13 (primary)
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of OSI letters)</i>	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> 10/16/13 – co-signed primary review
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> 10/16/13 (primary) 5/17/13 (filing)
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary <i>(include copies of OSI letters)</i>	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> 12/12/13 - co-signed primary review
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	Final CMC -December 12, 2013 Biopharm – May 16, 2013 CMC Filing – May 14, 2013
❖ Microbiology Reviews <input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input type="checkbox"/> Not needed November 14, 2013
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	Final CMC Review, page 69 – signed December 12, 2013
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷</i>)	Date completed: May 1, 2013 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

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/s/

MONSURAT O AKINSANYA
01/27/2014

Akinsanya, Lara

From: Akinsanya, Lara
Sent: Friday, October 18, 2013 1:43 PM
To: kwhite@salamandra.net
Cc: Akinsanya, Lara
Subject: Labeling - Information Request : Carton and Container for Decitabine/NDA 205582/Sun Pharma Global DUE November 8

Dear Kaylee White,

Please see below for requested changes to your carton and container labeling.

Drug container label

- a. Revise the statement (b) (4) that appears on the principal display panel of the container label to read “Single-Dose Vial – Discard Unused Portion”.
- b. Revise the strength to read “50 mg/vial” or “50 mg per vial”. The V in the vial should be lower case to increase the prominence of the strength 50 mg.
- c. Revise the statement (b) (4) to “For intravenous infusion only.” We recommend this to minimize the risk of administering the drug too fast based on our post marketing experiences.
- d. Revise the statement (b) (4) ” to read as follows:

Usual Dosage: See package insert.

This will create space for additional information to appear on the left side panel.

- e. Remove the statement (b) (4) on the left side panel as it is already stated on the principal display panel. This will create space for additional information to appear on the left side panel.
- f. Include instructions for reconstituting product and the resultant concentration on the left side panel. We acknowledge that this information is available on the carton, but our post marketing experiences indicate that container and cartons are frequently stored separately during pharmacy procurement process.
 - i. Add “Reconstitution: Reconstitute with 10 mL of Diluent for Decitabine for Injection. Each mL will contain 5 mg of decitabine. Further dilution is required. See package insert.”
- g. Include instructions on post-reconstitution expiration date and storage if space permits. We acknowledge that post-reconstitution instruction is available on the carton, but our post marketing experiences indicate that container and cartons are frequently stored separately during pharmacy procurement process.
- h. Remove the statement (b) (4).
- i. Decrease the prominence of the manufacturer’s logo on the principal display panel as it competes for prominence with information located at the bottom third of the principal display panel. Only the most important information such as name of the product, strength, and route of administration should be the most prominent information on the principle display panel.

Diluent container label

- a. Increase the prominence of the word “Diluent” so that it is the most prominent word on the label than “For Decitabine for Injection” to avoid drug-diluent confusion. One suggestion is to revise the statement to read as follows:

Diluent

For Decitabine for Injection

- b. Remove the statement [REDACTED] (b) (4)
- c. The background box behind “10 mL” should be in a different color to distinguish the diluent container from the drug container. We recommend this to minimize the risk of drug-diluent confusion.

Carton labeling

- a. Revise the statement [REDACTED] (b) (4) to “For intravenous infusion only.” We recommend this to minimize the risk of administering the drug too fast based on our post marketing experiences.
- b. Revise the statement [REDACTED] (b) (4) to “Further dilution is required. See package insert.”
- c. Under the section “This carton contains:” revise the statements below to read as follows:

This carton contains:

1 vial of Decitabine for Injection

1 vial of Diluent

- d. Add the statement “Single-dose vial” to the bottom of principal display panel.
- e. Debold the statement “Rx Only”.
- f. Relocate the statement “Final Concentration: The resultant solution will have a 5 mg/mL concentration and pH of 6.7 to 7.3.” to the side panel.
- g. On the bottom panel, add the statement “Further dilution is required. See package insert.” after the statement “Reconstitution: Reconstitute with 10 mL of Diluent for Decitabine for injection. Each mL will contain 5 mg of decitabine.”
- h. If space permits, move stability information to principal display panel. This may be achieved by decreasing the prominence of company logo and delete the statement [REDACTED] (b) (4).

Please respond by **Friday, November 8, 2013**.

Thank you

Lara

Lara (Monsurat) Akinsanya, M.S.
Senior Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
(301) 796-9634 (phone)
(301) 796-9849 (fax)

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/s/

MONSURAT O AKINSANYA
10/18/2013

Akinsanya, Lara

From: Akinsanya, Lara
Sent: Friday, October 18, 2013 1:51 PM
To: kwhite@salamandra.net; tsullivan@salamandra.net
Cc: Akinsanya, Lara
Subject: Labeling - Information Request : Package Insert for Decitabine/NDA 205582/Sun
Pharma Global DUE October 25

Dear Kaylee White,

Please find attached the FDA revised version of the PI for your review.



Please review the changes/comments and do the following to the same draft:

- Accept any changes that you agree with
- Edit over the ones that you do not agree with (do not reject any changes that the FDA proposed)

After you have made the changes, please email a revised PI (in tracked changes) to me by **Friday, October 25, 2013**.

Thank you
Lara

Lara (Monsurat) Akinsanya, M.S.
Senior Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
(301) 796-9634 (phone)
(301) 796-9849 (fax)

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MONSURAT O AKINSANYA
10/18/2013



NDA 205582

INFORMATION REQUEST

Sun Pharma Global FZE
c/o Salamandra, LLC
Attention: Karin A. Kook, Ph.D., Managing Director
One Bethesda Center
4800 Hampden Lane, Suite 900
Bethesda, MD 20814-2998

Dear Ms. Kook:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Decitabine for Injection.

We are reviewing the Quality section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Regarding  (b) (4)
process validation studies:



If you have any questions, contact Jewell Martin, Regulatory Project Manager, at (301) 796-2072.

Sincerely,

{See appended electronic signature page}

Ali Al Hakim, Ph.D.
Branch Chief
Branch II, Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

ALI H AL HAKIM
10/10/2013

Akinsanya, Lara

From: Akinsanya, Lara
Sent: Thursday, October 03, 2013 5:25 PM
To: kwhite@salamandra.net
Cc: Akinsanya, Lara
Subject: Non Clinical Information Request - Decitabine/NDA 205582/Sun Pharma Global
DUE October 11

Dear Kaylee White,

In regards to study No. BRT_12_081_TN "A 2-Dosing Cycle Intravenous Repeated Dose Toxicity Study in CD-1 Mice to Qualify the Impurities (b) (4) and (b) (4) Present in Decitabine Injection", please provide the following information by October 11, 2013:

1. Name, address and affiliation of the peer review pathologist.
2. A description of the codes (minimal, mild, moderate, severe, etc) used in the pathology report for grading the severity of findings, as well as the pathologist interpretation of the findings (pathology report).
3. An explanation for the absence of findings at the injection site. These include macroscopic and microscopic findings.
4. Historical data of pathology findings for the CD-1 mice breed at LAR, SPARC Ltd, Tandalja, Vadodara, India, if available.

Thank you
Lara

Lara (Monsurat) Akinsanya, M.S.
Senior Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
(301) 796-9634 (phone)
(301) 796-9849 (fax)

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/s/

MONSURAT O AKINSANYA
10/03/2013

Akinsanya, Lara

From: Akinsanya, Lara
Sent: Tuesday, October 01, 2013 2:52 PM
To: kwhite@salamandra.net
Cc: Akinsanya, Lara
Subject: CMC Information Request - Decitabine/NDA 205582/Sun Pharma Global DUE Oct 11

Dear Kaylee White,

We are reviewing your new NDA **205582** and would like to request a prompt written response to the below request for additional information (for time, please reply by e-mail in addition to submitting an amendment to the NDA) :

(b) (4)

Please respond by **Friday, October 11, 2013.**

Thank you
Lara

Lara (Monsurat) Akinsanya, M.S.
Senior Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
(301) 796-9634 (phone)
(301) 796-9849 (fax)

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/s/

MONSURAT O AKINSANYA
10/01/2013

Akinsanya, Lara

From: Akinsanya, Lara
Sent: Tuesday, September 17, 2013 3:32 PM
To: kwhite@salamandra.net
Cc: Akinsanya, Lara
Subject: Non Clinical Information Request - Decitabine/NDA 205582/Sun Pharma Global
DUE September 20

Dear Kaylee White,

We are reviewing your new NDA **205582** and would like to request a prompt written response to the below request for additional information (for time, please reply by e-mail in addition to submitting an amendment to the NDA) :

- We could not locate the dose formulation analysis conducted on Day 1 of cycle 1 and Day 5 of cycle 2 for study No. BRT_12_081_TN "A 2-Dosing Cycle Intravenous Repeated Dose Toxicity Study in CD-1 Mice to Qualify the Impurities (b) (4) and (b) (4) Present in Decitabine Injection" Please indicate the location or provide us with the report.

Please respond by **Friday, September 20, 2013**.

Thank you
Lara

Lara (Monsurat) Akinsanya, M.S.
Senior Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
(301) 796-9634 (phone)
(301) 796-9849 (fax)

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/s/

MONSURAT O AKINSANYA
09/17/2013

Akinsanya, Lara

From: Akinsanya, Lara
Sent: Wednesday, August 21, 2013 6:58 AM
To: kwhite@salamandra.net
Cc: Akinsanya, Lara
Subject: Information Request - Decitabine/NDA 205582/Sun Pharma Global DUE Aug 30

Dear Kaylee White,

We are reviewing your new NDA **205582** and would like to request a prompt written response to the below request for additional information (for time, please reply by e-mail in addition to submitting an amendment to the NDA) :

- *Please provide absolute values for all white blood cell types evaluated in study No. BRT_12_081_TN "A 2-Dosing Cycle Intravenous Repeated Dose Toxicity Study in CD-1 Mice to Qualify the Impurities (b) (4) and (b) (4) Present in Decitabine Injection.*

Please respond by **Friday, August 30, 2013**.

Thank you
Lara

Lara (Monsurat) Akinsanya, M.S.
Senior Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
(301) 796-9634 (phone)
(301) 796-9849 (fax)

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/s/

MONSURAT O AKINSANYA
08/21/2013



NDA 205582

FILING COMMUNICATION

Sun Pharma Global FZE
Attention: Karin A. Kook, PhD
Managing Director
Salamandra, LLC
One Bethesda Center
4800 Hampden Lane, Suite 900
Bethesda, MD 20814-2998

Dear Dr. Kook:

Please refer to your New Drug Application (NDA) dated March 25, 2013, received March 27, 2013 submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Decitabine for Injection, 50 mg/vial.

We also refer to your amendment dated May 24, 2013.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is January 27, 2014.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by December 16, 2013.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI) and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

If you have any questions, call Sherry Stewart, Regulatory Project Manager, at (301) 796-9618.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, MD
Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

ANN T FARRELL
06/04/2013



NDA 205582

NDA ACKNOWLEDGMENT

Sun Pharma Global FZE
Attention: Karin A. Kook, PhD
Managing Director
Salamandra, LLC
One Bethesda Center
4800 Hampden Lane, Suite 900
Bethesda, MD 20814-2998

Dear Dr. Kook:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Decitabine for Injection, 50 mg/vial

Date of Application: March 25, 2013

Date of Receipt: March 27, 2013

Our Reference Number: NDA 205582

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 26, 2013, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Hematology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, please call me at (301) 796-9618.

Sincerely,

{See appended electronic signature page}

Sherry A. Stewart, PharmD
Regulatory Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

SHERRY A STEWART
04/19/2013



PIND 114119

MEETING MINUTES

Sun Pharmaceuticals Industries Ltd. (SPIL)
C/O Salamandra, LLC
Attention: Karin A. Kook, Ph.D.
Managing Director
4800 Hampden Lane, Suite 900
Bethesda, MD 20814

Dear Dr. Kook:

Please refer to your Pre-Investigational New Drug Application (PIND) file for Decitabine injection.

We also refer to the teleconference between representatives of your firm and the FDA on February 6, 2012. The purpose of the meeting was to discuss the development plans to support an eventual NDA under Section 505(b)(2) of the Federal FD&C Act..

A copy of the official minutes of the teleconference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have questions, contact Marcus Cato, Regulatory Project Manager, at (301) 796-3903.

Sincerely,

{See appended electronic signature page}

Edvardas Kaminskas, M.D.
Deputy Director (Acting)
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B
Meeting Category: Pre-NDA

Meeting Date and Time: February 6, 2012, 12:00 PM – 1:00 PM (EST)
Meeting Location: White Oak Building 22, Conference Room: 1315

Application Number: PIND 114119
Product Name: Decitabine
Indication: Treatment of patients with myelodysplastic syndromes (MDS)
Sponsor/Applicant Name: Sun Pharmaceuticals Industries Ltd. (SPIL)

Meeting Chair: Edvardas Kaminskas, M.D.
Meeting Recorder: Marcus Cato, MBA

FDA ATTENDEES

Edvardas Kaminskas, M.D., Deputy Director (Acting)
Tamy Kim, Pharm.D., Associate Director for Regulatory Affairs
Albert Deisseroth, M.D., Clinical Team Leader (Acting)
Thomas Herndon, M.D., Medical Reviewer
Haleh Saber, Ph.D., Supervisory Pharmacologist
Shwu-Luan Lee, Ph.D, Pharmacologist
Bahru Habtemariam, Pharm.D., Clinical Pharmacology Reviewer
Angelica Dorantes, Ph.D., Biopharmaceutics Reviewer
Kimberly DeFronzo, RPh, MS, MBA, Safety Evaluator, DMEPA
Janice Brown, Ph.D., CMC Lead, OPS, ONDQA
Marcus Cato, MBA, Regulatory Project Manager

SPONSOR ATTENDEES

Dr. Wattanaporn Abramowitz
Dr. Subhas Bhowmick
Dr. N. Subramanian
Dr. Harry Ruan
Dr. Karin Kook

1.0 BACKGROUND

SPIL has developed Decitabine for Injection as a new formulation and presentation of the already approved product, Dacogen® (NDA 21-790). SPIL has manufactured to date three batches of drug product and three batches of diluent in May – July 2011 at a scale of (b) (4) (b) (4) respectively. These batches are currently under the stability program that was initiated according to an established ICH program. The proposed NDA will contain full CMC information for these batches to include 6-month accelerated stability results and 36-month long term stability results for the three registration batches of each drug product and diluent. An overview of the drug product is provided in the background package.

2. DISCUSSION

CHEMISTRY, MANUFACTURING, AND CONTROLS (CMC)

1. *Are the comparative studies performed with the proposed product and the RLD adequate to support the NDA?*

FDA Response:

The drug substance and lyophilized drug product information appears reasonable. However, the comparative studies for your product show that total impurities and impurity at (b) (4) fail your proposed limits upon reconstitution (see table 1.2:4) and when further diluted in 0.9% w/v sodium chloride solution to produce the admixture (see table 1.2:5). Based on the data submitted, your product is not stable upon reconstitution or further diluted in 0.9% w/v sodium chloride solution. In addition, it is noted that different acceptance criteria for assay and related substances are proposed for release and shelf-life for the drug product specification (p.16). Harmonize your proposed acceptance criteria to reflect a single specification for both release and shelf-life, and revise the proposed specification accordingly.

Discussion:

FDA advised that the in-use study should not be performed as a comparative study with Dacogen.

We recommend that you follow ICH Q1A(R2) where testing is performed on the constituted or diluted product through the proposed in-use period on primary batches at initial and final time points. The drug product should meet the proposed specification throughout shelf life and for the full extent of any in-use period.

The Sponsor plans to submit a proposal to (b) (4) impurities observed during the in-use period.

PHARMACOLOGY / TOXICOLOGY

2. *SPIIL seeks confirmation that no nonclinical studies are required for the NDA.*

FDA Response:

We agree that for a 505(b)(2) application, you may rely on the prior FDA finding of safety and effectiveness for the reference drug Dacogen, as reflected in Dacogen approved labeling. Therefore, additional nonclinical studies to assess the safety or pharmacology of decitabine will not be needed.

We remind you that the specifications for impurities in the drug product should be below the threshold defined in ICH Q3 B(R2) or the proposed specifications should be adequately justified based on clinical or nonclinical data. Alternatively, levels of these impurities may be justified based on those reported for the reference drug. In your NDA you should also justify the levels of residual solvents and novel excipients.

Also, see response to question 1 above.

Discussion:

None.

3. *Is the plan for preparation of the nonclinical sections of the NDA acceptable?*

FDA Response:

Yes.

Discussion:

None.

BIOPHARMACEUTICS AND CLINICAL PHARMACOLOGY

4. *Does the Division agree that the plan to request a waiver of in vivo studies is acceptable and that no additional biopharmaceutics / clinical studies are required for the NDA?*

FDA Response:

You may request a waiver from the CFR requirement to provide data from an acceptable in vivo bioequivalence (BE). Please include in your NDA submission the BE waiver (biowaiver) request and the complete information/data supporting such request. Please note that the acceptability of the biowaiver request is a review issue during the NDA.

Discussion:

None.

5. *Does the Division agree that SPIL does not need to include Sections 2.7.1 or 2.7.2 in the NDA?*

FDA Response:

Yes.

Discussion:

None.

CLINICAL SAFETY AND EFFICACY

6. *Does the Division agree that no clinical studies are required?*

FDA Response:

The answer to this question depends on whether a biowaiver can be granted. Please provide a plan for a method of administration of this drug so that the drug product remains in specification during reconstitution and further dilution.

Is the plan to limit the search of the published literature to the time period since the most recent version of the approved labeling for the reference product acceptable?

FDA Response:

Yes, the plan is acceptable.

Discussion:

None.

7. *SPIL proposes to prepare only the Clinical Overview and an Integrated Summary of Safety (ISS) and does not plan to include an Integrated Summary of Efficacy, a Summary of Efficacy (Section 2.7.3), or a Summary of Safety (2.7.4). Does the Division agree with this plan?*

FDA Response:

Yes, FDA agrees with this plan.

Additional Clinical Comment:

Please provide an explanation for the increase of the impurity

(b) (4)

(b) (4)

The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency's regulations at 21 CFR 314.54, and the October 1999 Draft Guidance for Industry "Applications Covered by Section 505(b)(2)" available at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>. In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions challenging the Agency's interpretation of this statutory provision (see Docket FDA-2003-P-0274-0015, available at <http://www.regulations.gov>)

If you intend to submit a 505(b)(2) application that relies for approval on FDA's finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a "bridge" between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified. If you intend to rely on literature or other studies for which you have no right of reference but that are necessary for approval, you also must establish that reliance on the studies described in the literature is scientifically appropriate. We encourage you to identify each section of your proposed 505(b)(2) application that is supported by reliance on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature.

If you intend to rely on the Agency's finding of safety and/or effectiveness for a listed drug(s) or published literature describing a listed drug(s) (which we consider to be reliance on FDA's finding of safety and/or effectiveness for the listed drug(s)), you should identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that 21 CFR 314.54 requires identification of the "listed drug for which FDA has made a finding of safety and effectiveness," and thus an applicant may only rely upon a listed drug that is the subject of an NDA approved under section 505(c) of the FD&C Act. The regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

Discussion:

None.

3.0 **PRESCRIBING INFORMATION**

Proposed prescribing information (PI) submitted with your application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.

Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm>. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

MANUFACTURING FACILITIES

To facilitate our inspectional process, the Office of Manufacturing and Product Quality in CDER's Office of Compliance requests that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

4.0 ISSUES REQUIRING FURTHER DISCUSSION

- None

5.0 ACTION ITEMS

Action Item/Description	Owner	Due Date
The Sponsor to submit a proposal to justify higher levels of impurities observed during the in-use period.	Sponsor	N/A

6.0 ATTACHMENTS AND HANDOUTS

- Sponsor e-mailed response/clarification

Thank you for your preliminary responses to our questions pertaining to decitabine. They are very clear and most do not require further discussion. This is to inform you that we intend to attend the meeting via telephone conference call as scheduled on Monday 6 February at 12:00 PM. We would like to discuss Question 1 (and the related Additional Clinical Comment).

The impurity in question (b) (4) is the (b) (4), (b) (4)
(b) (4) Stability of the reconstituted product and the final admixture will be supported by comparing three batches of the SPIL product and the RLD, each prepared and stored identically. The columns headed "Specifications" were erroneously included in Tables 1.2:4-1.2:6; these only apply to the finished product.

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

/s/

EDVARDAS KAMINSKAS
02/07/2012