

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
200795Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 200795

SUPPL #

HFD # 150

Trade Name N/A

Generic Name Gemcitabine Injection

Applicant Name Hospira, Inc.

Approval Date, If Known

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.

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:

d) Did the applicant request exclusivity?

YES NO

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

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?

No

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# 020509

Gemzar

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

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

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: Amy Tilley

Title: RPM

Date:

Name of Office/Division Director signing form: Amna Ibrahim, M.D.

Title: Deputy Director/DDOP/OODP/CDER

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

AMY R TILLEY
08/04/2011

AMNA IBRAHIM
08/04/2011



Debarment Certification

Gemcitabine Injection

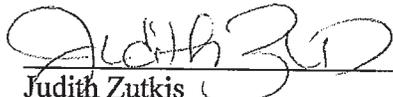
Section 306(k) of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. 335a(k)):

"Any application for approval of a drug product shall include

- (1) a certification that the applicant did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) in connection with such application, and

Hospira, Inc. hereby certifies that it did not and will not use, in any capacity, the services of any person debarred under section 306 of the Act in connection with this application.

Hospira, Inc. hereby states that it has no such convictions to list.



Judith Zutkis
Director, Global Regulatory Affairs
Hospira, Inc.
275 North Field Drive
Dept. 0389, Bldg. H2
Lake Forest, IL 60045-5046

2/19/09

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 200795 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: NA Established/Proper Name: Gemcitabine Dosage Form: Injection		Applicant: Hospira, Inc. Agent for Applicant (if applicable):
RPM: Amy Tilley		Division: DDOP
<p>NDA: 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>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>Mannitol is used in the freeze-dried RLD (b)(4) and therefore is not included in the solution dosage form. Sodium acetate is used in the RLD (b)(4) but was found not to be required in the proposed drug product. In addition, Hospira's proposed drug product is also available in 2 gram strength.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft 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: 8-4-11</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>8-10-11</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input type="checkbox"/> None CR 1-11-11

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.

<p>❖ 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 _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics²</p>	
<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"/> Rolling Review <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Direct-to-OTC </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"/> REMS not required </p> <p>Comments: Class 1 Resubmission</p>	
<p>❖ 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)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<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

² 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>
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist ³	Included
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(s) and date(s) CR 1-11-11 AP 8-4-11
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. 	7-18-11
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	1 st cycle 12-11-09 2 nd cycle 6-10-11
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	3-19-10 (RLD)

³ Fill in blanks with dates of reviews, letters, etc.
Version: 8/25/10

<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. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	
<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 	7-18-11
<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>) 	NA
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 9-24-10; 7-14-11 <input checked="" type="checkbox"/> DRISK 6-3-10 <input checked="" type="checkbox"/> DDMAC 7-22-11 <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 Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	RPM Filing Review 2-2-10
<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) 8-1-11 <input type="checkbox"/> Not a (b)(2) 8-4-11
<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 9-1-10 If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" 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
<ul style="list-style-type: none"> ❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>) 	Included

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 8/25/10

❖ Internal memoranda, telecons, etc.	Included
❖ 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 checked="" type="checkbox"/> No mtg
• 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>)	NA
❖ 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 1-11-11; 8-4-11
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 12-28-10; 7-27-11; 8-3-11
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	NA
• Clinical review(s) (<i>indicate date for each review</i>)	NA
• 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 MO Review 1-3-11
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input type="checkbox"/> None PMHS 11-17-10
❖ 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 Supporting Statement (<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
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested

⁵ Filing reviews should be filed with the discipline reviews.
Version: 8/25/10

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 checked="" type="checkbox"/> None
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>		<input type="checkbox"/> None 5-3-10; 7-21-11
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of DSI 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"/> None 12-8-10
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>		<input type="checkbox"/> None 12-8-10; 7-18-11
❖ 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
❖ DSI Nonclinical Inspection Review Summary <i>(include copies of DSI 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 checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>		<input type="checkbox"/> None 1-29-10; 2-2-10; 12-15-10; 7-15-11; 8-3-11
❖ Microbiology Reviews		<input type="checkbox"/> Not needed 2-10-10; 9-14-10; 12-2-10; 6-14-11
<input 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 (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>		
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>		<input 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>)		11-2-09
<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 type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<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 sites⁶</i>)		Date completed: 6-22-11 <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 type="checkbox"/> Completed <input type="checkbox"/> Requested <input checked="" type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

⁶ 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.
Version: 8/25/10

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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/s/

AMY R TILLEY
08/04/2011

From: Tilley, Amy
Sent: Friday, July 22, 2011 3:42 PM
To: 'Mohamed, Khaled' Khaled.Mohamed@hospira.com
Subject: NDA 200795 Gemcitabine - Acceptance of PI & Carton & Container Labels

Importance: High
Khaled,

This email is to inform you that we have accepted all the revisions in both your revised Product Insert and the Carton and Container Labels submitted on 7-18-11.

Regards.

Amy Tilley

Amy Tilley | Regulatory Project Manager | Division of Drug Oncology
Products, CDER, FDA

10903 New Hampshire Avenue, Room 2177 | Silver Spring, MD
20993

☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ amy.tilley@fda.hhs.gov



consider the environment before printing this e-mail

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/s/

AMY R TILLEY
07/22/2011

From: Kacuba, Alice
Sent: Wednesday, July 13, 2011 9:14 PM
To: 'khaled.mohamed@hospira.com'
Cc: Tilley, Amy
Subject: NDA 200795, Gemcitabine

Importance: High

Hi,

I am covering for Amy Tilley until 7-19-2011.

The purpose of this email is send you FDA requests for carton/container labeling changes for NDA 200795 for Gemcitabine.

- 1. All three strengths of the Gemcitabine Injection (200 mg/5.26 mL, 1 g/26.3 mL, and 2 g/52.6 mL) employ (b) (4) increasing their similarity, which can lead to selection errors. Although you revised the labeling to employ (b) (4) for Gemcitabine Injection 200 mg/5.26 mL to differentiate from (b) (4) employed for Gemcitabine Injection 2 g/52.6 mL, this differentiation (b) (4) is not sufficient to minimize the potential for selection errors. Use of a totally different color (b) (4) is recommended. Revise the labels and labeling to utilize different contrasting colors to minimize the potential for selection errors among the three different product strengths (i.e., only one strength should (b) (4))*
- 2. Add the expiration date and the lot number to the side panel in accordance with 21 CFR 201.17 and 21 CFR 201.100 (b)(6)*
- 3. We note that the container labels (b) (4) Typically, container labels use one bar code. (b) (4)*

4. *Increase the prominence of the statements “Single Use Vial. Discard Unused Portion” by relocating this statement from the side panel to the principle display panel. As currently presented, these statements are not prominent on the container labels; and thus, may be overlooked and may lead to the reuse of the single use vial. Increased prominence may be achieved by decreasing the prominence of the storage statement by debolding and printing the information in a smaller font. Although it is important to differentiate the storage conditions from the reference listed drug product Gemzar, it is also important to emphasize the product is packaged in to a single use vial and that the unused portion needs to be discarded in order to prevent reuse of the same vials of Gemcitabine.*

Package insert: Use the word “single vial” after the word intravenous in line 1, paragraph 5 under the description (11).

Please reply with your acceptance by Monday, July 18, 2011 by 11 AM. Sooner is better. I am covering for Amy Tilley until Tuesday, July 19, 2011.

Thank you.

Alice

Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Products
OND/CDER/FDA

301-796-1381

(f) 301-796-9845

alice.kacuba@fda.hhs.gov

*Consider setting your email font setting to at least 12 font.

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/s/

AMY R TILLEY
07/19/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION			
TO (Division/Office): CDER OSE CONSULT			FROM: Amy Tilley/RPM/OND/DDOP/301-796-3994		
DATE June 29, 2011	IND NO.	NDA NO. 505(b)(2) 200795	TYPE OF DOCUMENT PI & Carton/Container Labels	DATE OF DOCUMENT June 10, 2011	
NAME OF DRUG Gemcitabine Injection		PRIORITY CONSIDERATION Priority Class 1 Resubmission to CR 2 Month Clock	CLASSIFICATION OF DRUG 5	DESIRED COMPLETION DATE July 29, 2011	
NAME OF FIRM: Hospira, Inc.					
REASON FOR REQUEST					
I. GENERAL					
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY		<input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT		<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):	
II. BIOMETRICS					
STATISTICAL EVALUATION BRANCH			STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):			<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS					
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES			<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE					
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP			<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS					
<input type="checkbox"/> CLINICAL			<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: DDOP is requesting that OSE review the proposed product insert and carton and container labels for this 505(b)(2) NDA Class 1 Resubmission to CR. EDR Link: \\FDSWA150\NONECTD\4511071					
SIGNATURE OF REQUESTER Amy Tilley, RPM <i>{See appended electronic signature page}</i>			METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> E-MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER			SIGNATURE OF DELIVERER		

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/s/

AMY R TILLEY
06/29/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR DDMAC LABELING REVIEW CONSULTATION **Please send immediately following the Filing/Planning meeting**	
TO: CDER-DDMAC-RPM		FROM: (Name/Title, Office/Division/Phone number of requestor) Amy Tilley/RPM, OND/DDOP/301-796-3994	
REQUEST DATE June 29, 2011	IND NO.	NDA/BLA NO. 200795 505(b)(2)	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
NAME OF DRUG Gemcitabine Injection	PRIORITY CONSIDERATION Class 1 Resubmission to CR 2 Month Review Clock	CLASSIFICATION OF DRUG 5	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting)
NAME OF FIRM: Hospira, Inc.		PDUFA Date: August 10, 2011	
TYPE OF LABEL TO REVIEW			
TYPE OF LABELING: (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE(IFU)		TYPE OF APPLICATION/SUBMISSION <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	
REASON FOR LABELING CONSULT <input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION			
EDR link to submission:			
\\FDSWA150\NONECTD\4511071			
Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to DDMAC. Once the substantially complete labeling is received, DDMAC will complete its review within 14 calendar days.			
COMMENTS/SPECIAL INSTRUCTIONS:			
Mid-Cycle Meeting: NA (Class 1 Resubmission to a CR) Labeling Meetings: 7-12; 7-22; 7-26; 7-29; 8-2; and 8-8-11 Wrap-Up Meeting: 7-29-11 (if needed)			
SIGNATURE OF REQUESTER <i>{See appended electronic signature page}</i>			
SIGNATURE OF RECEIVER		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> eMAIL <input type="checkbox"/> HAND	

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/s/

AMY R TILLEY
06/29/2011



NDA 200795

**ACKNOWLEDGE --
CLASS 1 COMPLETE RESPONSE**

Hospira, Inc.
Attention: Khaled Mohamed
275 North Field Dr.
Dept. 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

We acknowledge receipt on June 10, 2011, of your June 10, 2011, resubmission to your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Gemcitabine Injection 200 mg/5.3 mL, 1 g/26.3 mL and 2 g/52.6 mL.

We consider this a complete, class 1 response to our January 11, 2011, action letter. Therefore, the user fee goal date is August 10, 2011.

If you have any questions, please contact me at 301-796-3994 or at amy.tilley@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Amy R. Tilley
Regulatory Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

AMY R TILLEY
06/28/2011

CMC MICRO & STERILITY ASSURANCE
REVIEW REQUEST

TO (Division/Office): **New Drug Microbiology Staff**
Jim McVey/Vera Viehmann

FROM: **Deborah Mesmer, ONDQA PM, 301.796.4023**

E-mail to: CDER OPS IO MICRO
Paper mail to: WO Bldg 51, Room 4193

PROJECT MANAGER (if other than sender):

REQUEST DATE 06/14/11	IND NO.	NDA NO. 200795	TYPE OF DOCUMENT Resubmission after CR	DATE OF DOCUMENT June 10, 2011 dated and stamped
NAMES OF DRUG Gemcitabine Injection	PRIORITY CONSIDERATION Not yet determined- 505(b)(2)	PDUFA DATE Depends on class determination 8/10/11 if Class I 12/10/11 if Class II	DESIRED COMPLETION DATE 7/20/11 if Class I 11/18/11 if Class II	

NAME OF APPLICANT OR SPONSOR: **Hospira**

GENERAL PROVISIONS IN APPLICATION

- | | |
|--|---|
| <input type="checkbox"/> 30-DAY SAFETY REVIEW NEEDED | <input type="checkbox"/> CBE-0 SUPPLEMENT |
| <input checked="" type="checkbox"/> NDA FILING REVIEW NEEDED BY: _June 21, 2011 (Class determination needed as soon as feasible._____ | <input type="checkbox"/> CBE-30 SUPPLEMENT |
| <input type="checkbox"/> BUNDLED | <input type="checkbox"/> CHANGE IN DOSAGE, STRENGTH / POTENCY |
| <input type="checkbox"/> DOCUMENT IN EDR | |

COMMENTS / SPECIAL INSTRUCTIONS:

ONDQA/DDOP is requesting a microbiology review of Hospira's Inc's NDA 200795 for Gemcitabine Injection indicated for the first-line treatment of metastatic breast cancer, inoperable, locally advanced or metastatic non-small cell lung cancer, and locally advanced or metastatic adenocarcinoma of the pancreas. In the amendment, Hospira provides:

- additional impurity assay validation data
- microbiological stability data to support post-dilution storage period-method validation (about 12 pages)
- draft labeling
- safety update information

Link to application: <\\FDSWA150\NONECTD\4511071>

Class I vs Class 2 determination needed as soon as feasible, as a Class I PDUFA would be 8/10/11.

Clinical Planning meeting scheduled for June 21, 2011- to determine if response is complete and what is the filing class.

Steven Langille was reviewer in previous cycle.

Chemistry reviewer: To be assigned
Project Manager for Quality: Debbie Mesmer
DDOP Project Manager: Amy Tilley

Please advise Debbie Mesmer and Amy Tilley of assigned reviewer.

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/s/

DEBORAH M MESMER
06/14/2011

MEMORANDUM



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 11 May 2011

TO: Amy Tilley
Regulatory Project Manager
OND/OODP/DDOP

FROM: Stephen E. Langille
Senior Microbiology Reviewer
New Drug Microbiology Staff

THROUGH: James McVey
Team Leader
New Drug Microbiology Staff

SUBJECT: Type A Sponsor Guidance Meeting for NDA 200-795

On April 7, 2011 Hospira Inc. submitted a Type A meeting package to discuss the FDA concerns provided in the January 11, 2011 complete response letter. Hospira Inc. asked the following question with regard to the microbiology deficiency associated with the proposed 24 hour post-dilution hold time:

In support of the 24 hour post-dilution/penetration storage time label claim for Gemcitabine Injection, Hospira executed this study per Agency instruction and recommendations in the Complete Response Letter. Does the Agency note any concerns with proposed approach? Would a full report of the study be sufficient upon submission of the response?

Hospira Inc. provided a Microbiology Method Validation Report addressing each of the following FDA recommendations for a post dilution hold time study:

- Employ a minimum countable inoculum to simulate potential microbial contamination that may occur during product dilution.
- Identify the time point at which the initiation of growth is clearly evident.
- Conduct sufficient replicates should be done to be able to identify when the titer is rising above the testing error of the no growth points. It is generally accepted that growth is evident when the population increases more than 0.5 Log₁₀.
- Run the test at the label's recommended storage conditions and conduct the test for

MEMORANDUM

2 to 3-times the label's recommended storage period. Use the label-recommended fluids.

- Periodic intermediate sample times are recommended. Challenge organisms may include strains described in USP <51> plus typical skin flora or species associated with hospital-borne infections.

Experiments were conducted in triplicate. The average cell counts for the test organisms are provided in the table below (obtained from p. 38 of the meeting package).

	<i>A. brasiliensis</i>	<i>C. albicans</i>	<i>E. coli</i>	<i>S. aureus</i>	<i>P. aeruginosa</i>	<i>M. luteus</i>
T ₀ Initial	50	79	63	74	60	45
T ₁ 6 hr	48	73	42	34	23	3
T ₂ 24 hr	47	83	21	0	6	0
T ₃ 48 hr	45	74	19	0	1	0
T ₄ 72 hr	44	71	10	0	1	0

A face to face meeting with the sponsor was held on 9 May 2011. The applicant asked if there were any concerns with the proposed approach to justify the 24 hour post dilution hold time at room temperature. Hospira Inc. was told that the proposed approach was adequate and that the procedure and results of the study should be included in the re-submission package for NDA 200-795. A complete review of the post-dilution dilution hold time study will be conducted in the next review cycle for NDA 200-795.

END

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/s/

STEPHEN E LANGILLE
05/31/2011

JAMES L MCVEY
05/31/2011
I concur.



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type A
Meeting Category: Guidance

Meeting Date and Time: May 9, 2011 from 2 – 3 pm
Meeting Location: WO Bldg 22, Rm 1419

Application Number: NDA 200795
Product Name: Gemcitabine Injection
Indication: Indicated for the first-line treatment of metastatic breast cancer, inoperable, locally advanced or metastatic non-small cell lung cancer, and locally advanced or metastatic adenocarcinoma of the pancreas.

Sponsor/Applicant Name: Hospira, Inc.
Meeting Request Date: March 3, 2011
Meeting BGP date: April 7, 2011

Meeting Chair: Sarah Miksinski, Ph.D., Branch Chief, ONDQA, DNDQA I
Meeting Recorder: Amy R. Tilley, Regulatory Project Manager

FDA ATTENDEES

Amna Ibrahim, M.D., Deputy Division Director
John R. Johnson, M.D., Lead Medical Officer
Sarah Pope Miksinski, Ph.D., Branch Chief, ONDQA, DNDQA I
Haripada Sarker, Ph.D., CMC Lead, ONDQA, DNDQA I
Joyce Crich, Ph.D., CMC Reviewer, ONDQA, DNDQA I, Branch II
Stephen Langille, Ph.D., Microbiology Reviewer
Derek Smith, Ph.D., Consumer Safety Officer, /OC/DMPQ
Shawn Gould, Ph.D., Consumer Safety Officer, /OC/DMPQ
Whitney Helms, Ph.D., Pharmacologist/Acting Supervisory Pharmacologist
Brenda Gehrke, Ph.D., Pharmacologist/Reviewer
Amy R. Tilley, Regulatory Project Manager

SPONSOR ATTENDEES

Attending from Lake Forest, Illinois

Eric Floyd, Vice President, Global Regulatory Affairs
Wendy Tian, Associate Director, Global Regulatory Affairs
Khaled Mohamed, Product Manager, Global Regulatory Affairs
Shawn Silvestri, Vice President, Global Pharma R&D
Edward W. Koo, Director Pre-clinical Development

Attending from Mulgrave, Australia

Darryl Whittaker, Ph.D., Director, Development Global Pharma R&D
Andrew Knill, R&D Technical Leader Formulation and Development
Tracey Mele, R&D Technical Leader Analytical and Stability

1.0 BACKGROUND

Gemcitabine Injection is an alternative to the currently approved Gemzar product offering a Sterile 'ready-to-use' solution by eliminating the reconstitution, for the first-line treatment of metastatic breast cancer, inoperable, locally advanced or metastatic non-small cell lung cancer, and locally advanced or metastatic adenocarcinoma of the pancreas.

The applicant of NDA 200795, Hospira, Inc. submits a Background Package to accommodate review of the actions taken by Hospira to address FDA concerns provided for NDA 200795 via the Complete Response issued January 11, 2011 by the Division of Drug Oncology Products. This package provides information in alignment with the original meeting request package provided on March 3, 2011 for a face-to-face Type A Meeting, which was granted and tentatively scheduled for May 9, 2011. The applicant's primary objective for this meeting is to gain the FDA's feedback on the approaches to address the issues identified in the Complete Response Letter dated January 11, 2011 in the areas of product quality, nonclinical, labeling, and facility inspection.

2.0 DISCUSSION

PRODUCT QUALITY

- 1) Hospira designed a validation approach to re-evaluate method linearity, accuracy and precision for the subject impurities for Method No. 6.320, Chromatographic Purity Test.

Does the proposed design/approach address FDA concerns to confirm suitability of the impurity method and validity of the test results being reported?

FDA Response:

The proposed design/approach to re-evaluate method linearity, accuracy and precision for the subject impurities for Method No. 6.320 appears to be reasonable in general for the proposed acceptance limits for [REDACTED] (b) (4)

[REDACTED] The final determination will be made during the NDA review process based on the totality of the provided data as it is a review issue, such as but not limited to, the accuracy of measured amount of isolated impurities by the proposed method, the stability of isolated impurities from initial isolation to the spiked experiment.

However, the proposed concentration ranges of impurities in the re-validation studies do not cover the concentrations of corresponding impurities in the lot U022750RA used in non-clinical toxicology studies. Therefore, the accuracy of measuring impurities [REDACTED] (b) (4) levels in non-clinical toxicology lot U022750RA is not supported by the proposed re-evaluation method. Refer to question No. 4. You must demonstrate the adequacy of the revalidated method No. 6.320 to support an accurate measurement of the higher level impurities in the non-clinical toxicology lot U022750RA.

Meeting Discussion:

The Agency reiterated that the sponsor should demonstrate the overall adequacy of the re-validated method No. 6.320 in the Complete Response submission. The Agency also recommended that the range be covered for linearity, precision and accuracy from the LOQ to 120% of the claimed levels for (b) (4) present in lot U022750RA.

MICROBIOLOGY

- 2) In support of the 24 hour post-dilution/penetration storage time label claim for Gemcitabine Injection, Hospira executed this study per Agency instruction and recommendations in the Complete Response Letter.

Does the Agency note any concerns with proposed approach?

FDA Response:

The proposed approach is acceptable.

Meeting Discussion:

None

- 3) Would a full report of the study be sufficient upon submission of the response?

FDA Response:

Yes, depending on the content of the report.

Meeting Discussion:

None

NONCLINICAL

- 4) Hospira reviewed the testing conducted at both Hospira and (b) (4) for lot U022750RA along with the corresponding method validation studies. The data generated under the new validation approach discussed in Item A confirmed the accuracy of the impurity levels originally measured in Lot U022750RA.

Does the Agency concur the toxicity evaluation conducted in Study 1632-08668 has adequately qualified the impurities for the proposed specification levels?

FDA Response:

Please see response to question 1. If the method is not validated during the review, then the specifications may need to be lowered or an additional non-clinical study may be necessary to support specifications.

Meeting Discussion:

FDA reiterated their response that if question 1 is adequately addressed the impurities will be qualified pending the review of the data.

LABELING

- 5) The RLD Package Insert was recently revised and posted 2/4/2011. As a result, Hospira will submit a revised product insert label, including a Word copy with changes tracked from the latest version submitted June 23, 2010, a clean Word copy, and structured product labeling (SPL).

Are these formats acceptable for continued label review?

FDA Response:

This appears to be acceptable.

Meeting Discussion:

None

FACILITY INSPECTIONS

- 6) Discussions with the API vendor and (b) (4) indicate that the inspection was conducted in July 2010.

Per (b) (4) the 483 questions conveyed were deemed minor and full response was provided within 15 business days.

It is unclear to (b) (4) and Hospira why the satisfactory resolution of these minor questions remains open.

It should be noted that Hospira provided two sites for the manufacture of the API via the vendor Jiangsu Hansoh in support of the registration process. Due to differences in API capacity between the two sites, Hospira intends to source API for commercial product production only from the Jiangsu Hansoh (b) (4) facility.

Therefore, we intend to modify the site responsibilities in Section 3.2.S.2.1 – Manufacturers to limit commercial manufacture and sourcing of API for commercial

production to the Jiangsu Hansoh (b) (4) facility. The (b) (4) site does not utilize any (b) (4)

Does the agency agree with this approach to progress to re-submittal?

FDA Response:

This approach is acceptable. The agency would like to clarify that the (b) (4) review is closed. The facility is currently classified as acceptable based on the Active Pharmaceutical Ingredient manufacturing facility profile class covered during the August 2010 inspection.

Meeting Discussion:

None

3.0 ISSUES REQUIRING FURTHER DISCUSSION

None

4.0 ACTION ITEMS

Action Item/Description	Owner	Due Date
SAFETY UPDATE	Hospira	As stated in the CR Letter dated 1-11-11, when you respond to the deficiencies you must include a safety update as described in 21 CFR 314.50(d)(5)(vi)(b).

6 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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/s/

AMY R TILLEY
05/09/2011

SARAH P MIKSINSKI
05/11/2011

Tilley, Amy

From: Tilley, Amy
Sent: Thursday, May 05, 2011 5:01 PM
To: 'Mohamed, Khaled'
Subject: NDA 200795 Gemcitabine - Preliminary Responses

Importance: High

Follow Up Flag: Follow up
Due By: Friday, May 06, 2011 12:00 AM
Flag Status: Flagged

Attachments: NDA 202795 Gemcitabine - Preliminary Commnets 5-2011.pdf

Khaled,

The attached consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for May 9, 2011 between Hospira and the Division of Drug Oncology Products. This material is shared to promote a collaborative and successful discussion at the meeting. The minutes of the meeting will reflect agreements, important issues, and any action items discussed during the meeting and may not be identical to these preliminary comments. If these answers and comments are clear to you and you determine that further discussion is not required, you have the option of canceling the meeting please (contact the RPM). **If you choose to cancel the meeting, this document will represent the official record.** If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda and/or change the format of the meeting (e.g., from face to face to telecon). It is important to remember that some meetings, particularly milestone meetings, are valuable even if the pre-meeting communications are considered sufficient to answer the questions. Note that if there are any major changes to your development plan/the purpose of the meeting/to the questions (based on our responses herein), we may not be prepared to discuss or reach agreement on such changes at the meeting. If any modifications to the development plan or additional questions for which you would like FDA feedback arise prior to the meeting, contact the Regulatory Project Manager to discuss the possibility of including these for discussion at the meeting.



NDA 202795
Gemcitabine - Preli..

Please let me know your decision to either keep or cancel the meeting as soon as possible. If you choose to keep the meeting, let me know which questions you would like to focus on during the meeting.

Kind Regards.

Amy Tilley

Amy Tilley | Regulatory Project Manager | Division of Drug Oncology Products, CDER,
FDA
10903 New Hampshire Avenue, Room 2177 | Silver Spring, MD 20993
☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ amy.tilley@fda.hhs.gov

PRODUCT QUALITY

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However, the proposed concentration ranges of impurities in the re-validation studies do not cover the concentrations of corresponding impurities in the lot U022750RA used in non-clinical toxicology studies. Therefore, the accuracy of measuring (b) (4) in non-clinical toxicology lot U022750RA is not supported by the proposed re-evaluation method. Refer to question No. 4. You must demonstrate the adequacy of the revalidated method No. 6.320 to support an accurate measurement of the higher level impurities in the non-clinical toxicology lot U022750RA.

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FDA Response:

Yes, depending on the content of the report.

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Does the agency agree with this approach to progress to re-submittal?

FDA Response:

This approach is acceptable. The agency would like to clarify that the (b) (4) (b) (4) review is closed. The facility is currently classified as acceptable based on the Active Pharmaceutical Ingredient manufacturing facility profile class covered during the August 2010 inspection.

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/s/

AMY R TILLEY
05/06/2011

MEMORANDUM OF TELECON

DATE: 1-10-11

APPLICATION NUMBERS: NDA 200795 & NDA 200582

BETWEEN:

Name: Eric Floyd
Phone: 888-459-7540
Representing: Hospira, Inc.

AND

Name: Amy Tilley & Allison Adams-McLean
DDOP, HFD-150

SUBJECT: To respond to Eric Floyd's 1-7-11 voicemail to Dr. Justice

BACKGROUND:

Excerpt from Eric Floyd's voicemail from 1-7-11:

"Good morning Dr. Justice Dr. Eric Floyd head of Regulatory at Hospira urgently need to speak with you regarding 2 drugs that are managed by Alice Kacuba. Gemcitabine NDA 200795 PDUFA date is 1-11-11 I am extremely concerned as we have had no correspondence no dialogue we have had a request for 2 players and neither have been responded to and we just have had no communication what-so-ever. We have received one Complete Response and I don't want to be in a situation where we receive another Complete Response in reference to something that could have been proactively addressed.

Second issue is NDA 200582 Topotecan also under Alice Kacuba's remit again no correspondence no dialogue can not get a return phone call. I'm very concerned about the lack of communication and the lack of transparency here. Can you call me at your earliest convenience...."

Excerpt from Alice's telephone log:

From Alice's phone log summary. Most current 1st.

Jan 5 at 2:40 pm VM from Eric Floyd at Hospira asking "Is there anything missing from the NDA?" Expecting action letter on Gem 1-11-2010 and Topotecan in Feb 2011." I did not return the call yet because.....I was thinking of what to tell him and would return it today.....I realize that 48 hours is too long to wait but...read on...

Dec 16 at 4:10 pm a VM was left which I returned at 6 PM and spoke with him. He asked if they would hear anything by Christmas and I said that we would be issuing a action letter by 1-11-2010. It would not be before Christmas.

Dec 9, 2010 3:30 pm which I returned at 5 PM. He asked if there was anything coming out on Topotecan and Gem. He went into a long song and dance about he was hired after the 2 NDAs were sent in and he was appalled by the quality of the cmc info submitted. It should not have been submitted like that. It is difficult relying on DMFs, etc. Hospira had set as a company goal to get AP for Gem and Topotecan by end of 2010 and if not he would be fired. I acknowledged that DMFs create a challenge to the sponsor and that I am surprised when I hear about company business practices.

I assured him that both Amy T and Alberta would send any IRs from the reviewers as soon as they got them. He acknowledged that both were good to work with.

Dec 1 at 12:59 pm which I returned that day. I didn't write down what time in my phone log. He asked for "guidance" on future 505b2s as they received 3 CRs this year from us. He explained that he just joined Hospira and said as he described it "the horse had already left the barn and the barn burned down" he said bad cmc was submitted. He said that Hospira only did generics and they never had issues with generics and got positive actions from generics. I told him I could only give general advice: use pre-NDA meetings, keep abreast of RLD, and 505b2 are not generics.

I stopped looking through my phone log at Thanksgiving time.

SUMMARY OF TELEPHONE CONVERSATION:

Dr. Justice stated he was not pleased with the miss-characterization regarding interactions or lack thereof with the regulatory team, specifically regarding Alice Kacuba. Alice has a telephone log of several communications between both herself and Eric Floyd.

Regarding NDA 200795 sponsor inquired about a status update on Gemcitabine. Sponsor stated they received a CMC Information Request on October 21, 2010 and they submitted their response on October 29, 2010. Sponsor also submitted Patent certification regarding the expiration of Patents on 12-6-10. Hospira also stated they submitted CMC responses on 8-5 and 8-16-10. Sponsor also inquired about the Micro and Labeling Reviews. The last labeling submission was sent by sponsor on 8-20-10.

ONDQA Branch Chief Sarah Pope Miksinski told the sponsor numerous times that the CMC and Micro Reviews were still ongoing. Amy Tilley stated there was no new information to report regarding labeling.

Regarding NDA 200582 Topotecan, the sponsor inquired why the December 2, 2010, submission was made a Class II, Dr Pope offered that the submission was re-evaluated and the Agency has reconsidered the classification and will made the submission a Class I with a PDUFA goal date February 2, 2011. Correspondence regarding classification change will be

submitted to the sponsor by Allison Adams-McLean. The sponsor inquired whether the PI for this NDA was acceptable, Allison Adams-McLean offered that updates regarding the PI will be forwarded to the sponsor.

Amy Tilley
Regulatory Project Manager

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/s/

AMY R TILLEY
03/14/2011

Tilley, Amy

From: Tilley, Amy
Sent: Tuesday, January 11, 2011 11:53 AM
To: 'Mohamed, Khaled'
Subject: NDA 200795 Gemcitabine - Complete Response Letter

Importance: High

Attachments: NDA 200795 Gemcitabine Complete Response Letter (2).pdf

Khaled,

Attached is a copy of the Complete Response Letter for NDA 200795 Gemcitabine. The official letter is forth coming in the mail.



NDA 200795
gemcitabine Complet.

Please confirm receipt of the copy of this letter via telephone.

Regards.

Amy Tilley

Amy Tilley | Regulatory Project Manager | Division of Drug Oncology Products, CDER,
FDA
10903 New Hampshire Avenue, Room 2177 | Silver Spring, MD 20993
☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ amy.tilley@fda.hhs.gov

 consider the environment before printing this e-mail

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/s/

AMY R TILLEY
01/11/2011

From: Cohen, Martin H
Sent: Monday, January 03, 2011 12:00 PM
To: Tilley, Amy
Subject: NDA 200795 Gemcitabine-Hospira – Is a Financial Disclosure Review needed?

Amy,

There were no new clinical studies performed. Therefore there is no financial disclosure needed.

Marty

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/s/

AMY R TILLEY
01/03/2011



NDA 200795

INFORMATION REQUEST

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 N. Field Drive
Dept: 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Gemcitabine Injection, 200 mg/5.3 mL, 1 gm/26.3 mL and 2 gm/52.6 mL.

We also refer to your August 5, 2010, and August 16, 2010, amendments and to the teleconference with FDA held on October 13, 2010.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a written response to these requests no later than October 28, 2010, so we may continue our evaluation of your NDA.

1. Clarify the following discrepancies:

- (a) Specify the name of the firm/site which actually conducted the "Structure Identification of the Major Unknown Impurity of Gemcitabine" study, since ChemWerth is designated only as an US agent (refer to Section 3.2.S.3.2).
- (b) Confirm the name for the firm/site which is responsible for drug product manufacture (refer to Section 3.2.P.2, P.15-31).
- (c) Clarify the relationship between Jiangsu Hansen and Jiangsu Hansoh. Confirm if both names apply to the same site and have the same assigned CFN FEI number. If not, provide updated information accordingly (refer to the name change in the amendment submitted on 05-AUG-2010).

2. Address the following items regarding the proposed starting material (b) (4)

- (a) Revise the acceptance specifications for the starting material (b) (4)
 - i. Include test methods and method numbers.
 - ii. Include an identification test (such as RRT) for each individual impurity under "Related Substances".

- (b) Provide structural information for each individual impurity under “Related Substances”.
- (c) Provide a brief description for each test method used in the acceptance specifications.

3. Address the following items regarding the raw materials:

- (a) Provide a detailed description for each identification test and propose an acceptance criterion for each raw material listed in Table 4 in Section 3.2.S.2.3.
- (b) Provide a comparison for test requirements (e.g., identification, purity and impurity levels) for these raw materials (solvents/reagents) for Chinese National Standards (or the supplier specifications) compared to the pertinent US grade standard.

4. Address the following items regarding the proposed in-process controls:

- (a) Provide an explanation for the following discrepancies noted in the tabular comparative summary of the processes (b) (4) (as submitted in the 05-AUG-2010 amendment), relative to the Narrative Description (Section 3.2.S.2.2).
 - (i) (b) (4) was mentioned in the 05-AUG-2010 amendment but was not included in the narrative description under Section 3.2.S.2.2 of the NDA submission.
 - (ii) (b) (4) do not match the corresponding procedures described in the narrative description in the NDA submission.

Also confirm which process is proposed for actual commercial production.

- (b) Include the batch size for each of the nine batches in the table of residual solvent batch analysis on page 35 in the 05-AUG-2010 amendment.
- (c) In general, the proposed TLC methodology is not quantitative in monitoring the in-process completion of each stage. The Agency recommends that you develop a quantitative TLC method (see USP <621>) or utilize other quantitative methods such as HPLC, with appropriate acceptance criterion, as in-process controls for each stage.

5. Revise Table II under 3.2.S.3.1 by removing the incorrect assignment (b) (4)

6. Address the following issues regarding your proposed analytical methods and related validation:

- (a) Clarify which GC method for residual solvents will be used as the regulatory test method in the drug substance specifications (e.g., the method specified in Report 923-SMV-001 versus that specified in Report VR-6-60603-E-0802). Include the method identification number for the proposed GC method.
- (b) Report VR-6-60603-E-0802 for residual solvent validation by Jiangsu Hansoh was drafted on 31-JUL-2009 and was approved on 21-AUG-2009. Provide an explanation for the omission of this report in the original NDA.

7. Include proposed acceptance criteria for each residual solvent (b) (4) in the drug substance specifications.
8. Due to the potential impact of temperature variations on overall drug substance quality, provide the shipping storage temperature conditions on the proposed Packaging Label for Gemcitabine Hydrochloride.
9. Based on your 16-AUG-2010 amendment, (b) (4) is not an excipient in your proposed drug product formulation. Revise Table 3.2.P.3.2-2, Table 3.2.P.4.1-1, and Table 3.2.P.4.4-1 by removing (b) (4) which is currently listed as an excipient.
10. Address the following regarding your proposed analytical methods for impurities in the drug product, and provide additional validation data or justification as appropriate:
 - (a) Develop and use working reference standards for specified impurities for gemcitabine (b) (4)
 - (b) Determine the true RRF values for any specified impurities (b) (4)
 - (c) Re-establish appropriate concentration ranges for the specified impurities for validation of linearity, accuracy, and precision based on ICH Q2B. Your validation data indicate that you validated one impurity (b) (4) but the concentration range was outside of the range recommended by ICH Q2B.
11. Regenerate the batch analysis for drug product lots based on Deficiency #10 above.
12. Revise the proposed acceptance criteria for impurities (individual and total) in the drug product specification based on the re-analyzed batch data.
13. Re-evaluate the batch analysis data from stability studies based on revised HPLC analytical methods for impurities (see Deficiency #10 above). Revise the proposed expiration dating period based on the valid batch analysis for stability studies and the revised specifications for impurities (see Deficiency #12) if needed.
14. Considering that there is no overage or overfill used in the manufacture or formulation of the drug product, the amount of gemcitabine injection in each vial is the exact amount as claimed in the label. Provide supporting data and justification to quantitatively demonstrate that there is no "dead volume" for each of the three containers. If there is any volume lost in the dose preparation and delivery process, confirm the exact amount and provide pertinent supporting data.

If you have any questions, call Deborah Mesmer, Regulatory Health Project Manager, at 301-796-4023.

Sincerely,

{See appended electronic signature page}

Richard T. Lostritto, Ph.D.
Director
Division of New Drug Quality Assessment I (DNDQA I)
Office of New Drug Quality Assessment (ONDQA)
Center for Drug Evaluation and Research

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/s/

RICHARD T LOSTRITTO
10/21/2010

REQUEST FOR CONSULTATION

TO (Office/Division): **PMHS, CDER PMHS**

FROM (Name, Office/Division, and Phone Number of Requestor): **Amy Tilley,
OND/DDOP, 301-796-3994**

Rosemary Addy – Pediatric contact

DATE
October 8, 2010

IND NO.

NDA NO.
200795

TYPE OF DOCUMENT
**505(b)(2) NDA Product
Insert**

DATE OF DOCUMENT
June 23, 2010

NAME OF DRUG
Gemcitabine Injection

PRIORITY CONSIDERATION
Priority

CLASSIFICATION OF DRUG
5

DESIRED COMPLETION DATE
October 20, 2010

NAME OF FIRM: **Hospira, Inc.**

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input checked="" type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|---|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILTY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|--|--------------------------------------|
| <input checked="" type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|--|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult request is to ask for PMHS to assist with review of the pediatric language regarding negative studies in the proposed gemcitabine 505(b)(2) label for NDA 200795. Currently proposed section 8.4 on Pediatric use for pending NDA 200795 reads as follows:

"The safety and effectiveness of Gemzar in pediatric patients has not been established. Gemzar was evaluated in a Phase 1 trial. in pediatric patients with refractory leukemia and determined that the maximum tolerated dose was 10 mg/m²/min for 360 minutes three times weekly followed by a one-week rest period. Gemzar was also evaluated in a Phase 2 trial in patients with relapsed acute lymphoblastic leukemia (22 patients) and acute myelogenous leukemia (10 patients) using 10 mg/m²/min for 360 minutes three times weekly followed by a one-week rest period. Toxicities observed included bone marrow suppression, febrile neutropenia, elevation of serum transaminases, nausea, and rash/desquamation, which were similar to those reported in adults. No meaningful clinical activity was observed in this Phase 2 trial."

DDOP proposes removal of information protected by pediatric exclusivity in the Gemzar label, which is not expected to affect safe use of the drug. DDOP recommends that for 505b2 drugs for Gemzar, only the sentence “The safety and effectiveness of Gemzar in pediatric patients has not been established” remain in the label at this time.

Please provide your comments in 7 business days due to time constraints for this NDA and a meeting with the following individuals to discuss this issue.

Participants for Meeting scheduled 10-21-10 from 11 am - Noon Rm 2201:

John Jenkins, Sandy Kweder, PMHS Reps, Reps for 505b2, Liz Dickinson, Kim Dettelbach, Robert Justice, Amna Ibrahim, John Johnson, Marty Cohen, Amy McKee (DDOP pediatric oncologist), Alice Kacuba, Tamy Kim, Amy Tilley, Frank Cross, Modupe Fagbami, Patricia Cortazar, and Kristen Snyder.

A separate email will contain the Product Insert for your review along with a copy of this consult.

If possible, assign the same reviewer that has reviewed docetaxel with the same issue.

SIGNATURE OF REQUESTOR Amy Tilley {See appended electronic signature page}	METHOD OF DELIVERY (Check one) <input type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

AMY R TILLEY
10/08/2010

Tilley, Amy

From: Greeley, George
Sent: Monday, October 04, 2010 3:28 PM
To: Tilley, Amy
Cc: Salis, Olga
Subject: NDA 200-795 Gemcitabine

Importance: High

Attachments: 1_Pediatric_Record.pdf

Hi Amy,

The Gemcitabine full waiver was reviewed by the PeRC PREA Subcommittee on September 1, 2010.

The Division recommended a full waiver because the disease/condition does not exist in children

The PeRC agreed with the Division to grant a full waiver for this product. The pediatric record is attached as confirmation of the PeRC's review.



*_Pediatric_Record
.pdf (62 KB)...

Thank you.

George Greeley
Regulatory Health Project Manager
Pediatric and Maternal Health Staff
FDA/CDER/OND
10903 New Hampshire Avenue
Bldg. 22, Room 6467
Silver Spring, MD 20993-0002
Phone: 301.796.4025
Email: george.greeley@fda.hhs.gov

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NDA 200795

INFORMATION REQUEST

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 N. Field Drive
Dept: 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Gemcitabine Injection, 200 mg/5.3 mL, 1 gm/26.3 mL and 2 gm/52.6 mL.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a written response to these requests no later than September 30, 2010, so we may continue our evaluation of your NDA.

Provide the following product quality microbiology information or a reference to its location within the new drug application:

[Redacted] (b) (4)

[Redacted] (b) (4)

3. Diagrams and/or detailed descriptions of thermocouple and biological indicator placement within [Redacted] (b) (4)

4. The results of media fill lot number T010068A (p. 83 of section 3.2.P.3.5) indicate that only [Redacted] (b) (4) Provide an explanation as to why [Redacted] (b) (4) during this simulation.

5. The results of the most recent [Redacted] (b) (4) processing simulations conducted in filling rooms 9, 12, and 16.

If you have any questions, call Deborah Mesmer, Regulatory Health Project Manager, at 301-796-4023.

Sincerely,

{See appended electronic signature page}

Sarah Pope Miksinski, Ph.D.
Chief, Branch II
Division of New Drug Quality Assessment I (DNDQA I)
Office of New Drug Quality Assessment (ONDQA)
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

HARIPADA SARKER

08/27/2010

I am signing the document on behalf of Sarah Pope Miksinski



NDA 200795

**REVIEW EXTENSION –
MAJOR AMENDMENT**

Hospira, Inc.
Attention: Khaled Mohamed
Product Manager, Global Regulatory Affairs
275 N. Field Drive
Lake Forest, IL 60045

Dear Mr. Mohamed:

Please refer to your December 11, 2009 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Gemcitabine Injection, 200 mg/5.3 mL, 1 g/26.3 mL, 2 g/52.6 mL.

On August 4 and August 6, 2010, we received your August 3 and August 5, 2010, solicited major amendments to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is January 11, 2011.

In addition, we are establishing a new timeline for communicating labeling changes and/or postmarketing requirements/commitments in accordance with "PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012." If major deficiencies are not identified during our review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by December 14, 2010.

If you have any questions, call Amy Tilley, Regulatory Project Manager, at 301-796-3994.

Sincerely,

{See appended electronic signature page}

Amy R. Tilley
Regulatory Health Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
08/25/2010

From: Adams, William M
Sent: Friday, August 20, 2010 12:41 PM
To: Tilley, Amy
Cc: Pope Miksinski, Sarah; Lostritto, Richard T; Crich, Joyce
Subject: RE: Re: NDA 200795 - review extension
ONDQA is recommending an extension of the review clock for the following reason.

A major amendment was filed in parts on 04 Aug 2010 and on 06 Aug 2010. Based on the preliminary review of these amendments, the CMC reviewer will require additional time to reach a conclusion of approvability or not approvability for the NDA.

mike adams, acting Branch Chief

From: Crich, Joyce
Sent: Wednesday, August 11, 2010 8:49 PM
To: Adams, William M
Cc: Pope Miksinski, Sarah; Tilley, Amy; Lostritto, Richard T
Subject: RE: Re: NDA 200795 - review extension

Mike,

Please confirm by email that you agree to recommend the review team to extend review on NDA 200795 with following reason, as I can only provide information to you, the decision/recommendation needs to be made at branch level. If the recommendation can not be made on extension, then I need to adjust my other working load so there might be a possibility to read through and review the amendment as listed in my email below before the initial PDUFA date.

Thanks,

Joyce

From: Crich, Joyce
Sent: Monday, August 09, 2010 12:20 PM
To: Adams, William M
Cc: Pope Miksinski, Sarah
Subject: Re: NDA 200795 - review extension

Mike,

Per your request, I put rough information together for you to modify (to get a approval from our division?). Once you are done, would you please inform Amy Tilley in email by end of the day, I should appreciate very much. Thanks, Joyce

Justifications of Extending Review Clock for NDA 200795

The first IR letter with 20 comments for both DS and DP was issued on July 2, 2010, the responses from Hospira were received on August 4, 2010 for DP part and on August 6, 2010 for DS part. In the response to the first IR letter, Hospira informed the agency for multiple changes in drug substance with supplemental documents: (b) (4)

(b) (4) the specifications for the starting material; English translations for all the Certificate of Analysis from Chinese for raw materials; in-process control for the manufacturing of drug substance with batch data; test methods and the acceptance criteria for each stage of the manufacturing process; batch analysis for manufacturing process validation; acceptance criteria for the intermediate specifications; validation for analytical method for residual solvents and batch analyses for residual solvents; analyses of new drug substance batches manufactured from the starting material from the new vendor. Hospira also informed the agency in the response for the changes in drug product: acceptance criteria for assay and impurities; analytical method validation for chromatography purity; real time stability data; etc.

Note: the PDUFA day for NDA 200795 is Oct 11, 2010

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
08/23/2010

From: Tilley, Amy
Sent: Thursday, August 19, 2010 1:39 PM
To: 'Mohamed, Khaled'
Subject: NDA 200795 Gemcitabine - Carton & Container Information Request

Importance: High
Khaled,

This Information Request has been generated as per our TCON on 8-18-10 between you, myself and Alice Kacuba. During the TCON you agreed to send in your carton and container label revisions to us both officially and as a courtesy email no later than 8-31-10.

We look forward to receiving your revisions.

Regards.

Amy Tilley

Amy Tilley | Regulatory Project Manager | Division of Drug Oncology
Products, CDER, FDA
10903 New Hampshire Avenue, Room 2177 | Silver Spring, MD
20993

☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ amy.tilley@fda.hhs.gov



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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
08/19/2010

MEMORANDUM OF TELECON

DATE: August 17-10

APPLICATION NUMBER: NDA 200795

BETWEEN:

Name: Khaled Mohamed
Phone: 224-212-4909
Representing: Hospira, Inc.

AND

Name: Alice Kacuba & Amy Tilley
DDOP, HFD-150

SUBJECT: Sponsor revised carton and container labels

This TCON was the result of a telephone conversation from Khaled Mohamed from Hospira with Amy Tilley on 8-17-10. During this telephone conversation, Khaled wanted to let the Agency know they would be updating their carton and container labels and wanted to send the submission to us after they received the Agency's next revisions to the product insert. Alice Kacuba and Amy Tilley telephoned Khaled back on 8-17-10 to notify him that he must not wait until the Agency sends additional revisions to the product insert, but rather, Hospira must officially submit any additional revisions to their carton and container labels no later than August 31, 2010. Khaled Mohamed from Hospira, Inc. agreed.

Amy Tilley
Regulatory Project Manager
Division of Drug Oncology Products

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
08/18/2010



NDA 200795

INFORMATION REQUEST

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 N. Field Drive
Dept: 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Gemcitabine Injection, 200 mg/5.3 mL, 1 gm/26.3 mL and 2 gm/52.6 mL.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a written response to these requests in the same submission as your response to the correspondence dated July 2, 2010, so we may continue our evaluation of your NDA.

1. Since [REDACTED]^{(b)(4)} it should not be included in Table 1, Qualitative Composition in 3.2.P.1. Provide the detection limit for [REDACTED]^{(b)(4)} in the drug product. Justify whether [REDACTED]^{(b)(4)} needs to be included in the regulatory drug product specifications as an impurity or residue with an established acceptance criterion for its level.
2. Provide compatibility study data for Gemcitabine Injection product (38 mg/mL) in PVC bag without diluent, to support your statement of 24 hours stability for drug product in an empty PVC bag.

If you have questions, call Deborah Mesmer, Regulatory Health Project Manager, at (301) 796-4023.

Sincerely,

William M. Adams for 27 July 2010

Sarah Pope Miksinski, Ph.D.
Chief, Branch II
Division of New Drug Quality Assessment I (DNDQA I)
Office of New Drug Quality Assessment (ONDQA)
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

WILLIAM M ADAMS

07/27/2010

William Adams, acting for Sarah Pope Miksinski



NDA 200795

INFORMATION REQUEST

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 N. Field Drive
Dept: 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

Please refer to your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Gemcitabine Injection, 200 mg/5.3 mL, 1 gm/26.3 mL and 2 gm/52.6 mL.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a written response no later than July 30, 2010, in order to continue our evaluation of your NDA.

Drug Substance

1. Provide solubility test data for drug substance in the following solvents: water, ethanol, chloroform, acetone, and methanol.
2. Regarding the starting material (b) (4)
 - (a) Provide scientific rationale for using the following testing methods for in-process control of manufacturing (b) (4)

(b) (4)
 - (b) Revise the proposed acceptance criteria for (i) Assay from NLT (b) (4) to NLT (b) (4) and (ii) Total Impurities from NMT (b) (4) to NMT (b) (4) to minimize the level of impurity (b) (4) in the drug substance. Alternatively, demonstrate your manufacturing capability of removing these impurities from (b) (4) during the DS manufacturing process.
 - (c) Correct the discrepancies for the assay acceptance criterion between the proposed specification and the Description of the Manufacturing Process for (b) (4)

For example, Table 1 of 3.2.S.2.3.1 indicated assay NLT (b) (4) while assay NLT (b) (4) is indicated on page 25 in the Description of the Manufacturing Process in 3.2.S.2.2.

- (d) Identify and characterize each of the “Any other impurity” listed in the specification. This should include, but is not limited to impurities (b) (4). Indicate the level of each “Any other impurity” reported in Table 2 (b) (4) in 3.2.S.2.3.1.
 - (e) Provide structural information for the impurities at RRT 2.87 (NMT (b) (4)) and RRT 2.91 (NMT (b) (4)) listed in the specification.
 - (f) Provide the batch number for the material addressed in Figure 1 (b) (4) in 3.2.S.2.3.1 and its corresponding impurity profile (name, level, etc.).
3. Regarding the control of raw materials used in Gemcitabine Hydrochloride manufacture:
- (a) Provide an accurate translation for the Certificate of Analysis from Chinese to English for each raw material listed in Table 4 in 3.2.S.2.3.
 - (b) Revise the acceptance specifications for each of the raw materials listed in Table 4 in 3.2.S.2.3 to confirm identity, key physical property, purity, inorganic and organic impurities, etc.
4. Regarding in-process control:
- (a) Provide quantitative acceptance criteria for the in-process controls; refer to Table 10 (3.2.S.2.2.2) and Table 1 (3.2.S.2.4).
 - (b) Provide a detailed description of the test methods (e.g., TLC solvent system) and the acceptance criteria for each stage of the manufacturing process.
 - (c) Provide historical batch data in tabular format with yields, purity, and impurities data for each isolated intermediate and the final drug substance according to the sequence of the manufacturing process for drug substance
 - (d) Revise the acceptance criteria for the intermediate specifications to reflect the batch data reported for intermediates from both manufacturing sites. Provide the results from the validation studies for the HPLC methods used for intermediate testing. (Refer to the ICH Q2(A) and ICH Q2(B) guidances).
 - (e) Provide a summary comparing the processes in the proposed critical steps and include supporting data from both sites (b) (4)
 - (f) Provide data to demonstrate the capability of your manufacturing process to remove residual solvents (b) (4) used during the synthesis.
5. The assigned molecular weight (b) (4) for the adduct does not correlate to (b) (4). Please provide the correct data.
6. Clarify the role and responsibility of ChemWerth Inc, Jiangsu Hansen, and Hospira. For an example, 3.2.S.2.1 lists ChemWerth Inc as the U.S. agent for Jiangsu Hansen,

however ChemWerth provided the report “Structure Identification of the Major Unknown Impurity of Gemcitabine” dated May, 2004. (Refer to 3.2.S.3.2).

7. Regarding the analytic methods and analytical method validations,
 - A. For residual solvents:
 - (a) Provide a side-by-side comparison of analytical test results for residual solvents by GC methods 7.143 and 7.147.
 - (b) Provide explanations for the discrepancy in the values for limit of detection (LOD) and limit of quantitation (LOQ) in Tables 7 and 8 on pages 64-65 and Table 8 on page 12 in 3.2.S.4. The values in Tables 7 and 8 appear to be lower than the limits in Table 8.
 - (c) Provide the specific LOD and LOQ values for each residual solvent method reported in the batch analysis data (Table 1 in 3.2.S.4.5).
 - (d) We recommend that you follow ICH Q2(A), ICH Q2(B) and USP <467> to develop and validate your GC methods for residual solvents (e.g. signal-to-noise ratio for LOD and LOQ, linearity range, etc.).
 - B. Provide justification for measuring S/N (Signal to Noise ratio) manually rather than by using instrumental integration in the validation study for the Related Substance Test Method.
8. Regarding the specification and batch analysis data for Drug Substance:
 - (a) Revise the proposed acceptance criteria for the residual solvent, isopropanol, based on the reported batch analysis data.
 - (b) Provide a criterion for each residual solvent used in the manufacturing process.
 - (c) Provide batch analysis data for each residual solvent used in the manufacturing process.
9. Regarding the reference standards:
 - (a) Develop reference standards for impurities (b) (4) Alternatively, provide justification why a reference standard for these impurities is not needed. Refer to 3.2.S.5.1 and 3.2.S.5.2.
 - (b) Include ¹H and ¹³C NMR studies in the characterization and standardization of the working reference standard against the USP reference standard. Refer to 3.2.S.5.2.
10. Provide the shipping storage conditions (for example, temperature, etc.) on the proposed Packaging Label for Gemcitabine Hydrochloride.

Drug Product

1. Propose an acceptable pH range after drug product dilution with normal saline based on your test data.
2. Clarify the role and responsibility of Mayne Pharm, Limited regarding drug product manufacture. Refer to pages 15-31 of 3.2.P.3.

3. Revise the proposed acceptance criterion for Assay from (b) (4) labeled content to (b) (4) labeled content based on the USP Monograph standard for Gemcitabine hydrochloride for Injection.
4. Revise the proposed acceptance criteria for impurities (individual and total) in the drug product specification based on the batch analysis data.
5. Identify the batch numbers for materials used to obtain the “Typical Chromatogram of an Assay Working Standard Solution” and for the “Typical Chromatogram of an Impurity Working Standard Solution”, respectively. Refer to Figure 1 & Figure. 2 in 3.2.P.5.2.
6. Provide the calculation to demonstrate how the linearity ranges for the assay and impurities methods were determined. Refer to 3.2.P.5.3.
7. Provide the calculation to justify the concentration ranges used in the accuracy study for the assay and impurities methods. Refer to 3.2.P.5.3.
8. Provide a reference standard for each specified impurity in the drug product specification.
9. Revise the shelf life specification and regulatory drug product specification to use a single criterion for each test. This should include the identification test. Submit the updated regulatory drug product specification in a tabular format. Refer to 3.2.P.8.1, Table 4 and 3.2.P.8.2, Table 1.
10. Your proposed (b) (4) expiration dating period under refrigerated storage conditions is not supported by your real time stability data. We do not recommend that you relax the assay range from the USP compendia standard of (b) (4) to your proposed (b) (4) in order to accommodate a high level of impurities/degradation products in support of your proposed expiration dating period.

If you have any questions, call Deborah Mesmer, Regulatory Health Project Manager, at 301-796-4023.

Sincerely,

{See appended electronic signature page}

Sarah Pope Miksinski, Ph.D.
Chief, Branch II
Division of New Drug Quality Assessment I (DNDQA I)
Office of New Drug Quality Assessment (ONDQA)
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

WILLIAM M ADAMS

07/02/2010

William Adams, acting for Sarah Pope Miksinski

Tilley, Amy

From: Tilley, Amy
Sent: Tuesday, June 15, 2010 2:03 PM
To: 'Mohamed, Khaled'
Subject: NDA 200795 Gemcitabine Injection - PI & Carton & Container Label Revisions

Importance: High

Attachments: FDA LABELING COMMENTS revs from 5-25-10 mtg.doc; PI w-tracked changes- FDA revised 5-25-10.doc; carton label FDA revised 5-25-10.pdf; container label FDA revised 5-25-10.pdf

Khaled,

Attached are the PI and the Carton & Container Labels along with a document to help clarify the revisions.



FDA LABELING
OMMENTS revs fro.



PI w-tracked
changes- FDA revi...



carton label FDA
revised 5-25-...



container label FDA
revised 5-...

Please respond back with your revisions by June 24, 2010.

Regards.

Amy Tilley

Amy Tilley | Regulatory Project Manager | Division of Drug Oncology Products, CDER,
FDA

10903 New Hampshire Avenue, Room 2177 | Silver Spring, MD 20993

☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ amy.tilley@fda.hhs.gov



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FDA LABELING COMMENTS:

We have evaluated the container labels and carton labeling for Gemcitabine Injection. The evaluation of these container labels and carton labeling resulted in the identification of several areas of needed improvement. Please revise labels and labeling as follows.

A. All Labels and Labeling (200 mg/5.26 mL, 1 g/26.3 mL, 2 g/52.6 mL)

1. All three strengths of the Gemcitabine Injection (200 mg/5.26 mL, 1 g/26.3 mL, and 2 g/52.6 mL) employ (b) (4) increasing their similarity, which can lead to selection errors. Revise the labels and labeling to utilize different contrasting colors to minimize the potential for selection errors among the three different product strengths.

2. Present information on the labels and labeling in a manner to foster clarity and comprehension. Furthermore, linking relevant phrases to one another helps to ensure that important steps conveyed on the labels and labeling are not omitted due to fragmentation of those steps. Accordingly, please revise the information on the label and labeling as follows.

a. (b) (4)

(b) (4) Revise the presentation so that the total drug content statement appears on a solid one color background which clearly displays '200 mg/5.26 mL or xx g/mL.'

b. Delete the term (b) (4) from the labels and labeling (e.g., on principal display panel beneath the concentration statement) when used in conjunction with the dosage form. The correct dosage form for this product is injection.

a. Place the statement "Discard Unused Portion" immediately after or on the same line as the statement "Single Use Vial."

b. Delete the term (b) (4) from the container label and carton labeling. This term is unnecessary and occupies space.

c. Decrease the prominence of the "Rx only" statement. As currently presented, it is more prominent than the concentration statement. Additionally relocate the Rx only statement to a less prominent location on the principle display panel such as the upper right corner (b) (4) or lower right or left corner.

d. The labels and labeling have references to both Gemcitabine and Gemcitabine Hydrochloride USP. We recommend using consistent terminology when referring to the active ingredient.

3. Because the referenced listed drug, Gemzar is a different dosage form with different storage recommendations, ensure that the information on proper storage for this product is prominent. Increase the prominence of the statement "Store at 2° to 8° C (36° to 46° F) by relocating it to the principal display panel below the route of administration statement. Do not use the red font for the storage requirements, since red font should only be used to emphasize critical statements such as "Caution: Cytotoxic Agent."

4. Delete the (b) (4) statement.
5. Prominence can be achieved by printing the statement in bold letters, and/or using a bigger font if space permits.

B. Container Labels (200 mg/5.26 mL, 1 g/26.3 mL, 2 g/52.6 mL)

1. (b) (4) and replace with the statement
"For Dosing and Administration: See package insert." (b) (4)

2. Delete (b) (4)

C. Carton Labeling (200 mg/5.26 mL, 1 g/26.3 mL, 2 g/52.6 mL)

1. (b) (4)

2. (b) (4)

3. Delete (b) (4) and replace with the statement
"For Dosing and Administration: See package insert." (b) (4)

4. (b) (4)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
06/15/2010

From: Tilley, Amy
Sent: Monday, March 29, 2010 1:12 PM
To: 'Mohamed, Khaled'
Subject: NDA 200795 Gemcitabine Inj - Information Request Submit new updated PI

Importance: High

Hello Khaled,

The PI from Lilly the RLD, has been converted into PLR Format and was approved on 3/19/10. You can find their most current PI on the Drugs @ FDA website. Please revise your PI to match that of the RLD and officially resubmit it to us. Could you please send me an email letting me know when you are ready to resubmit the revised PI?

Thank you.

Amy Tilley

Amy Tilley | Regulatory Project Manager | Division of Drug Oncology
Products, CDER, FDA

10903 New Hampshire Avenue, Room 2177 | Silver Spring, MD
20993

☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ amy.tilley@fda.hhs.gov



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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
03/29/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION			
TO (Division/Office): CDER OSE CONSULT			FROM: Amy Tilley/RPM/OND/DDOP/301-796-3994		
DATE March 2, 2010	IND NO.	NDA NO. 505(b)(2) 200795	TYPE OF DOCUMENT PI & Carton/Container Labels	DATE OF DOCUMENT December 11, 2009	
NAME OF DRUG Gemcitabine Injection		PRIORITY CONSIDERATION Priority	CLASSIFICATION OF DRUG 5	DESIRED COMPLETION DATE August 31, 2010	
NAME OF FIRM:					
REASON FOR REQUEST					
I. GENERAL					
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY		<input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT		<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):	
II. BIOMETRICS					
STATISTICAL EVALUATION BRANCH			STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):			<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS					
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES			<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE					
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP			<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS					
<input type="checkbox"/> CLINICAL			<input type="checkbox"/> PRECLINICAL		
<p>COMMENTS/SPECIAL INSTRUCTIONS: DDOP is requesting that OSE review the proposed product insert and carton and container labels for this 505(b)(2) NDA. Please find the submission in the EDR for any other pertinent information you may need to complete your review (path to link:) \\FDSWA150\NONECTD\4248458</p> <p>Clinical Reviewer: Martin Cohen, M.D; PM: Amy Tilley. To facilitate your review, I will send via email the labels and PI once the RLD PI from Lilly (PLR conversion which is currently being revised) has been finalized.</p>					
SIGNATURE OF REQUESTER Amy Tilley, RPM <i>{See appended electronic signature page}</i>			METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> E-MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER			SIGNATURE OF DELIVERER		

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
03/02/2010

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO:

CDER-DDMAC-RPM

FROM: (Name/Title, Office/Division/Phone number of requestor)

Amy Tilley/RPM, OND/DDOP/301-796-3994

REQUEST DATE
March 2, 2010

IND NO.

NDA/BLA NO.
505(b)(2) 200795

TYPE OF DOCUMENTS
(PLEASE CHECK OFF BELOW)

NAME OF DRUG

Gemcitabine Injection

PRIORITY CONSIDERATION

Priority

CLASSIFICATION OF DRUG

5

DESIRED COMPLETION DATE

(Generally 1 week before the wrap-up meeting)

August 31, 2010

NAME OF FIRM:

Hospira, Inc.

PDUFA Date: October 11, 2010

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:

(Check all that apply)

- PACKAGE INSERT (PI)
- PATIENT PACKAGE INSERT (PPI)
- CARTON/CONTAINER LABELING
- MEDICATION GUIDE
- INSTRUCTIONS FOR USE (IFU)

TYPE OF APPLICATION/SUBMISSION

- ORIGINAL NDA/BLA
- IND
- EFFICACY SUPPLEMENT
- SAFETY SUPPLEMENT
- LABELING SUPPLEMENT
- PLR CONVERSION

REASON FOR LABELING CONSULT

- INITIAL PROPOSED LABELING
- LABELING REVISION

EDR link to submission:

<\\FDSWA150\NONECTD\4248458>

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: May 17, 2010

Labeling Meetings: April 27, 2010, May 10, 2010, & May 25, 2010

Wrap-Up Meeting: September 7, 2010

Post Decision Mtg: October 7, 2010

SIGNATURE OF REQUESTER: Amy Tilley, RPM *{See appended electronic signature page}*

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)

eMAIL

HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
03/02/2010



NDA 200795

FILING COMMUNICATION

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 North Field Dr.
Dept. 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

Please refer to your new drug application (NDA) dated December 11, 2009, received December 11, 2009, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Gemcitabine Injection, 200 mg/5.3 mL, 1 g/26.3 mL, 2 g/52.6 mL.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is Standard. Therefore, the user fee goal date is October 11, 2010.

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 September 13, 2010.

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.

If you request a full waiver, we will notify you if the full waiver is denied and a pediatric drug development plan is required.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult the Division of Drug Oncology Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Amy Tilley, Regulatory Project Manager, at 301-796-3994.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

ALICE KACUBA
02/23/2010



NDA 200795

FILING COMMUNICATION

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 North Field Dr.
Dept. 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

Please refer to your new drug application (NDA) dated January 25, 2010, received January 26, 2010, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Gemcitabine Injection, 200 mg/5.3 mL, 1 g/26.3 mL, 2 g/52.6 mL.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is Standard. Therefore, the user fee goal date is October 11, 2010.

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 September 13, 2010.

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.

If you request a full waiver, we will notify you if the full waiver is denied and a pediatric drug development plan is required.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult the Division of Drug Oncology Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Amy Tilley, Regulatory Project Manager, at 301-796-3994.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

ROBERT L JUSTICE
02/17/2010



NDA 200795

NDA ACKNOWLEDGMENT

Hospira, Inc.
Attention: Khaled M. Mohamed
Sr. Associate, Global Regulatory Affairs
275 North Field Dr.
Dept. 0389, Bldg. H2-2
Lake Forest, IL 60045-5046

Dear Mr. Mohamed:

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: Gemcitabine Injection, 200 mg/5.3 mL, 1 g/26.3 mL, 2 g/52.6 mL

Date of Application: December 11, 2009

Date of Receipt: December 11, 2009

Our Reference Number: NDA 200795

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 February 9, 2010 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.

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 Drug Oncology 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>

If you have any questions, call Amy Tilley, Regulatory Project Manager, at 301-796-3994.

Sincerely,

{See appended electronic signature page}

Amy R. Tilley
Regulatory Health Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
01/27/2010

REQUEST FOR CONSULTATION

TO (Office/Division): Patrick Marroum CDER/OPS/ONDQA,
Angelica Dorantes CDER/OPS/ONDQA

FROM (Name, Office/Division, and Phone Number of Requestor): Terrance
Ocheltree, Ph.D. through Debbie Mesmer, Office of
New Drug Quality Assessment, 301 796-4023

DATE
January 26, 2010

IND NO.

NDA NO.
200795

TYPE OF DOCUMENT
NDA original submission

DATE OF DOCUMENT
December 11, 2009

NAME OF DRUG
Gemcitabine Injection

PRIORITY CONSIDERATION
Not yet determined-
505(b)(2)

CLASSIFICATION OF DRUG
Oncology

DESIRED COMPLETION DATE
Review completed by
March 11, 2010 if priority;
May 11, 2010 if standard
review

NAME OF FIRM: Hospira

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input checked="" type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: A Biopharmaceutics review is requested to determine if the applicant's request for a biowaiver is acceptable.

Link to application: \\FDSWA150\NONECTD\4248458

Joyce Critch, Ph.D. is the primary CMC reviewer. (Terrance Ocheltree, PAL)

Martin Cohen, M.D. is the medical reviewer

Amy Tilley is the OND RPM

Debbie Mesmer is the ONDQA RPM

Please notify Debbie Mesmer of the assigned Biopharm reviewer.

SIGNATURE OF REQUESTOR {See appended electronic signature page}		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND	
PRINTED NAME AND SIGNATURE OF RECEIVER		PRINTED NAME AND SIGNATURE OF DELIVERER	

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

DEBORAH M MESMER
01/26/2010

TERRANCE W OCHELTRREE
01/26/2010

REQUEST FOR CONSULTATION

TO (Office/Division): David Hussong/Jim McVey/Sylvia Gantt
NEW DRUG MICROBIOLOGY STAFF
OC/OO/CDER/OPS/NDMS - HFD-805

FROM (Name, Office/Division, and Phone Number of Requestor): Terrance Ocheltree, Ph.D. through Debbie Mesmer, Office of New Drug Quality Assessment, 301 796-4023

DATE
January 13, 2010

IND NO.

NDA NO.
200795

TYPE OF DOCUMENT
NDA original submission

DATE OF DOCUMENT
December 11, 2009

NAME OF DRUG
Gemcitabine Injection

PRIORITY CONSIDERATION
Not yet determined-
505(b)(2)

CLASSIFICATION OF DRUG
Oncology

DESIRED COMPLETION DATE
Review completed by
March 11, 2010 if priority;
May 11, 2010 if standard
review

NAME OF FIRM:

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: ONDQA/DDOP is requesting to have a microbiology review of Hospira's Inc's new NDA 200795 for Gemcitabine Injection indicated for the first-line treatment of metastatic breast cancer, inoperable, locally advanced or metastatic non-small cell lung cancer, and locally advanced or metastatic adenocarcinoma of the pancreas.

Link to application: \\FDSWA150\NONECTD\4248458

Joyce Critch, Ph.D. is the primary CMC reviewer. (Terrance Ocheltree, PAL)

Martin Cohen, M.D. is the medical reviewer

Amy Tilley is the OND RPM

Debbie Mesmer is the ONDQA RPM

SIGNATURE OF REQUESTOR { See appended electronic signature page }		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND	
PRINTED NAME AND SIGNATURE OF RECEIVER		PRINTED NAME AND SIGNATURE OF DELIVERER	

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200795	ORIG-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

DEBORAH M MESMER
01/13/2010

TERRANCE W OCHELTRIE
01/14/2010

October 30, 2009

1) List of Questions

- a) Is the available literature and toxicology study adequate to qualify the impurity profile demonstrated under long term storage conditions for the proposed Gemcitabine Injection solution drug product to proceed with resubmission of the NDA?

FDA Response:

(b) (4) and (b) (4) are qualified according to your current specification. The shelf life of the product will be a review issue.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
IND-106215	GI-1	HOSPIRA INC	GEMCITABINE INJECTION (38MG/ML)

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/s/

AMY R TILLEY
10/30/2009