CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202356Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 202356 SUPPL # HFD # 150

Trade Name: N/A

Generic Name: Docetaxel Injection

Applicant Name: Pfizer Labs

Approval Date, If Known: March 13, 2014

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES ☒ NO ☐

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

505(b)(2)

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

YES ☐ NO ☒

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

Product is pharmaceutically equivalent to the RLD. Only has a different qualitative and quantitative formulation. Applicant was granted a waiver for bioequivalence

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#	020449 (RLD)	Taxotere (docetaxel) Injection
NDA#	201195 203551 022234 201525 022534	Docetaxel Injection
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:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

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

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

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

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

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

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

YES ☐ NO ☐

If yes, explain:

==========

Name of person completing form: **Modupe Fagbami**
Title: Regulatory Project Manager, DOP1
Date: March 7, 2014

Name of Office/Division Director signing form: **Amna Ibrahim**
Title: Deputy Director, DOP1

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

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

/s/

MODUPE O FAGBAMI
03/13/2014

AMNA IBRAHIM
03/14/2014

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 202356 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: N/A Established/Proper Name: Docetaxel Injection Concentrate Dosage Form: Injection		Applicant: Pfizer Labs Agent for Applicant (if applicable):
RPM: Modupe Fagbami		Division: DOP1

NDAs and NDA Efficacy Supplements:

NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

(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.)

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)):

NDA 20-449 Taxotere 40 mg/ml (Sanofi-aventis; approved 5-14-1996)

Provide a brief explanation of how this product is different from the listed drug.

1. 1 vial formulation that does not require a pre-mix step and is ready for immediate dilution and administration. Active pharmaceutical ingredient is anhydrous docetaxel instead of trihydrate docetaxel used in Taxotere.

2. Use of polypropylene vial instead of glass vial.

☐ This application does not reply upon a listed drug.
☐ This application relies on literature.
☐ This application relies on a final OTC monograph.
☐ This application relies on (explain)

For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft[2] to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.

On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.

☒ No changes ☐ Updated Date of check: 3-13-2014

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.

❖ Actions

[1] The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 5) lists the documents to be included in the Action Package.
[2] For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., nrew listed drug, patent certification revised).

• Proposed action • User Fee Goal Date is February 14, 2013	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None Complete response issued on 2-29-2012; and 2-14-2013
❖ 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 _____	☐ Received
❖ Application Characteristics [3]	

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only):

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
- ☐ Accelerated approval (21 CFR 314.510)
- ☐ Restricted distribution (21 CFR 314.520)

Subpart I
- ☐ Approval based on animal studies

BLAs: Subpart E
- ☐ Accelerated approval (21 CFR 601.41)
- ☐ Restricted distribution (21 CFR 601.42)

Subpart H
- ☐ Approval based on animal studies

☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

REMS:
- ☐ MedGuide
- ☐ Communication Plan
- ☐ ETASU
- ☐ MedGuide w/o REMS
- ☐ REMS not required

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action (by OEP)	☐ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

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

❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *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.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application)? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes
• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(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.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• 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.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• 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) ☐ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [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).	☐ No paragraph III certification
• [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). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☒ Verified

Version: 1/27/12

- [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).*

(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? (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). *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*).* *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.*	☐ Yes ☒ No
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist[4]	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 *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s) 3rd cycle: Approval Action: 3-13-14 2nd cycle: Complete Response: 2-14-13 1st cycle: Complete Response: 2-29-12

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

Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	Sponsor proposed labeling 1-27-2014
• Original applicant-proposed labeling	Sponsor proposed labeling (3rd Cycle) 1-27-14; 1-10-14; 9-12-13 Sponsor proposed labeling (2nd Cycle) 8-30-12; 8-14-12 Sponsor proposed labeling (1st cycle) 4-29-11
• Example of class labeling, if applicable	N/A
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☒ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	Sponsor proposed labeling 9-12-13
• Original applicant-proposed labeling	Sponsor proposed labeling (3rd Cycle) 1-27-14; 1-10-14; 9-12-13 Sponsor proposed labeling (2nd Cycle) 8-30-12; 8-14-12 Sponsor proposed labeling (1st cycle) 4-29-11
• Example of class labeling, if applicable	N/A
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	Sponsor proposed labeling (3rd Cycle) 9-12-2013 Sponsor proposed labels (2nd Cycle) 8-14-12 Sponsor proposed labels (1st cycle) 4-29-11
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s)* • *Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name.*	N/A
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☒ Labeling Review: 3-12-14; RPM 1-23-14(SRPI Review) ☒ DMEPA: 3-7-2014, and 2-21-2014 (3rd cycle); 2-1-13 (2nd cycle); 1-20-12 (1st cycle) OSE/DPV: 2-14-14 (3rd cycle) ☒ DMPP/PLT (DRISK) 3-4-14 (3rd cycle;1-29-13 (2nd cycle); 1-17-12 (1st cycle) ☒ ODPD (DDMAC) 2-21-14 (3rd cycle); 1-25-12 (1st cycle)

	☐ SEALD ☐ CSS ☐ Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews *(e.g., RPM Filing Review[5]/Memo of Filing Meeting) (indicate date of each review)* ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment *(indicate date)*	RPM Filing Review: N/A for 3rd cycle RPM Filing Review: N/A for 2nd cycle RPM Filing Review: 6-9-11 Cleared for Action (3rd Cycle) 2-3-2014 Cleared for Action (2nd cycle) 1-30-13 Cleared for TA Action (1st cycle)1-30-12 505(b)(2) Assessment :2-27-14
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	x Included 3-14-14
❖ Application Integrity Policy (AIP) Status and Related Documents http://www fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC N/A If PeRC review not necessary, explain: 505(b)(2); PREA not triggered • Pediatric Page/Record *(approvals only, must be reviewed by PERC before finalized)*	N/A ☐ Included
❖ 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 *(include certification)*	☒ Verified, statement is acceptable
❖ Outgoing communications *(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)*	3rd Cycle IR e-mail: 3-6-14 IR e-mail: 2-25-14 IR e-mail: 1-23-14 IR e-mail: 1-15-2014 IR e-mail: 1-6-14 (checked on 2-5-14) IR e-mail: 12-23-13 IR e-mail: 10-30-13 Ackn. Letter: 10-01-13 (2nd cycle) IR email: 12-19-12 IR email: 12-10-12 IR letter: 11-16-12

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

	IR email: 10-9-12 Ackn letter: 9-7-12 IR email: 8-20-12 IR email: 8-15-12 (1st cycle) IR email: 11-29-11 IR letter: 11-18-11 IR letter: 10-7-11 IR letter: 8-5-11 Filing letter: 7-6-11 Ack letter: 5-16-11
❖ Internal memoranda, telecons, etc.	Mid-cycle mtg minutes 10-11-11 Planning mtg mins 5-23-11
❖ Minutes of Meetings	
• Regulatory Briefing *(indicate date of mtg)*	☒ No mtg
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☐ No mtg
• EOP2 meeting *(indicate date of mtg)*	☐ No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	Pre-IND mtg 11-1-10
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available *(do not include transcript)*	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	3-12-14 (3rd cycle) 2-14-13 (2nd cycle); 2-29-12 (1st cycle)
Cross-Discipline Team Leader Review *(indicate date for each review)*	3-11-14 (3rd cycle) 1-31-13 (2nd cycle); 2-6-12 (1st cycle)
PMR/PMC Development Templates *(indicate total number)*	☒ None
Clinical Information[6]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	3rd cycle reviews 2-26-14 (co-signed primary clinical review) 2nd cycle reviews: 1-13-13 (Co-signed primary clinical review) 1st cycle reviews: 1-17-12 (Co-signed primary clinical review)

[6] Filing reviews should be filed with the discipline reviews.

• Clinical review(s) *(indicate date for each review)*	3rd cycle reviews: 2-26-14 2nd cycle reviews: 1-13-13 1st cycle reviews: 1-17-12
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☒ and include a review/memo explaining why not *(indicate date of review/memo)*	505(b)(2)
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ Not applicable
❖ Risk Management • REMS Documents and Supporting Statement *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	N/A N/A ☒ None
❖ OSI Clinical Inspection Review Summary(ies) *(include copies of OSI letters to investigators)*	☒ None requested
Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☐ None
Clinical Microbiology Review(s) *(indicate date for each review)*	☐ None
Biostatistics ☒ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☐ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ None
Statistical Review(s) *(indicate date for each review)*	☐ None

Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☐ None 3rd cycle reviews: 1-28-14 (co-si gned primary review) 2nd cycle reviews: 1-22-13 (co-signed primary review) 1st cycle reviews: 1-13-12 (co-signed primary review)
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 3rd cycle reviews: 1-28-14 12-16-13 (filing review) 2nd cycle reviews: 1-22-13 1st cycle reviews: 1-13-12 6-7-11 (filing review)
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	☒ None

Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ None
• Supervisory Review(s) *(indicate date for each review)*	☐ None 3rd cycle reviews: 2-24-14 (co-signed primary review) 2nd cycle reviews: 1-15-13 (co-signed primary review) 1st cycle reviews: 2-14-12 (co-signed primary review) 1-26-12 (co-signed primary review)
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None 3rd cycle reviews: 2-24-14 2nd cycle reviews: 1-15-13 1st cycle reviews: 2-14-12 1-26-12 6-2-11 (filing review)
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary *(include copies of OSI letters)*	☒ None requested

Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ None
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☐ None 3rd cycle reviews: 1-24-14 (co-signed primary review) 2nd cycle reviews: 1-30-13 (co-signed primary review) 1st cycle reviews: 2-23-12 (co-sign primary review) 1-25-12 (co-sign primary review)
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☐ None 3rd cycle reviews: 1-24-14 2nd cycle reviews: 2-11-13 1-30-13 11-19-12 (biopharm review) 1st cycle reviews: 2-23-12 1-25-12 12-23-11 (biopharm review) 6-7-11 (filing review) 6-7-11 (biopharm filing review) 6-3-11 (CMC filing review)
❖ Microbiology Reviews ☐ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) *(indicate date of each review)*	☐ Not needed 3rd cycle reviews: 10-01-2013 2nd cycle reviews: N/A 1st cycle reviews: 1-25-12 6-3-11 (micro filing review)
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	1-25-12
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	

❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout) *(date completed must be within **2 years** of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[7])*	Date completed: Overall OC Recommendation on 11-8-13-3rd cycle; 2-8-13 (2nd cycle) ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER *(date of most recent TB-EER must be within **30 days** of action date) (original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

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

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/

MODUPE O FAGBAMI
03/14/2014

From: Fagbami, Modupe
Sent: Thursday, March 06, 2014 6:30 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 Docetaxel FDA Revisions to Package Insert and PPI
Importance: High

Hi Tricia,

Please find attached the FDA Revisions to the Package Insert as updated at the t-con (FDA and Pfzer) today 3/6/2014.

The updates from DMEPA have been added to it also, therefore there is no need for an Information Request as promised at the meeting.

Throughout the label, please ensure that there are 2 spaces after each period.

Docetaxel Pfizer
- Docetaxel ...

I am also attaching the FDA revisions to the PPI.

Kindly ensure that you incorporate the updated PPI to the PI without loosing the formatting.

Docetaxel
ction NDA 20235

As promised at the t-con, please send the updated Package Insert to me on or before COB, Friday, March 7, 2014.

Please let me know if you have any questions.

Thank you

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348

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MODUPE O FAGBAMI
03/06/2014

From: Fagbami, Modupe
Sent: Tuesday, February 25, 2014 1:08 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 Docetaxel FDA Revisions to Package Insert
Importance: High

Hi Tricia,

Please find attached the FDA revisions to the package insert for NDA 202356.

NDA
-submission me

If the revisions are acceptable to you, kindly accept the all the changes and send me the clean copy on or before, 12:00 noon EST, Friday, February 28, 2014.

Please ensure that the formatting are also done.

Let me know if you have any questions.

Thank you.

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348
Fax: 301-796-9845

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MODUPE O FAGBAMI
02/25/2014

From: Fagbami, Modupe
Sent: Monday, January 06, 2014 2:47 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 Docetaxel
Importance: High

Dear Tricia,

Reference your September 12, 2013, submission for NDA 202356 Docetaxel.

Please note that a new supplement has just been approved for your Reference Listed Drug, Taxotere, on December 13, 2013.

Kindly send your label using this just RLD's approved label.

We expect this updated label to be submitted to the FDA on or before COB, Friday, January 10, 2014 to enable us keep with your present goal date of March 13, 2014.

Let me know if you have any questions.

Thank you

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348
Fax: 301-796-9845

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/s/

MODUPE O FAGBAMI
02/05/2014

From: Fagbami, Modupe
Sent: Thursday, January 23, 2014 3:39 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 Docetaxel Information Request
Importance: High

Dear Tricia,

Please find the following formatting deficiencies to your PI:

1. Highlights Limitation Statement:

Name of drug product is not in UPPER CASE letters

2. Initial U S Approval in Highlights:

Not followed by 4-digit representing the year such as "XXXX"

3. Table of Content:

Table of content is not in two columns.

4. Adverse Reactions:

- **Clinical Trials:**

Verbatim statement not included. See below:

"Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice."

- **Post-marketing Experience:**

Verbatim statement not included. See below:

"The following adverse reactions have been identified during post approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the drug exposure."

Kindly update your PI appropriately and submit to the FDA on or before 12:00 noon EST, January 27, 2014.

Let me know if you have any questions.

Thank you.

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348
Fax: 301-796-9845

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/s/

MODUPE O FAGBAMI
01/23/2014

From: Fagbami, Modupe
Sent: Wednesday, January 15, 2014 2:58 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 Docetaxel Clinical Information Request
Importance: High

Dear Tricia,

Based on the current FDA Orange Book patent and exclusivity data (Accessed 14 Jan 2014), there are no unexpired patents or pediatric exclusivity for the referenced product, Taxotere (NDA 20449). Pediatric exclusivity appears to have expired on November 13, 2013. Please revise the proposed Pfizer docetaxel prescribing information (USPI) to include the most current pediatric use information in the Taxotere USPI.

We expect the response to this information request on or before COB, Wednesday, January 22, 2014.

Kindly let me know if you have any questions.

Thank you.

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348
Fax: 301-796-9845

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/s/

MODUPE O FAGBAMI
01/15/2014

From: Fagbami, Modupe
Sent: Monday, December 23, 2013 10:04 AM
To: 'Racanelli, Tricia'
Subject: NDA 202356 Docetaxel Additional Clinical Pharmacology Information Request
Importance: High

Dear Tricia,

We are requesting additional clarification regarding your response to clinical pharmacology information request dated October 30, 2013. In this response, you provided the EXCEL spreadsheet (and a PDF version) referenced in the previously submitted report entitled “Projected Blood Concentrations of Ethanol and Propylene Glycol Following Infusion of Docetaxel.”

- Could you please provide line-by-line explanation of the sheet titled "(b) (4)". For example, it is unclear what the elimination half-life is for the "Longer T1/2" and "Shorter T1/2" calculations.

- Could you also justify the selection of the half-life values chosen in the "(b) (4)" sheet.

- Could you provide an additional prediction of blood ethanol and propylene glycol concentrations at 30 min post infusion, when a T1/2 of 2 hrs is assumed, and when a T1/2 of 4 hrs is assumed?

Please send the response to this request by COB, Monday, January 6, 2014.

Let me know if you have any questions.

Thank you

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348
Fax: 301-796-9845

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/s/

MODUPE O FAGBAMI
12/23/2013

From: Fagbami, Modupe
Sent: Wednesday, October 30, 2013 11:13 AM
To: 'tricia.racanelli@pfizer.com'
Subject: NDA 202356 Docetaxel Injection Clinical Pharmacology Information Request
Importance: High

Dear Tricia,

Below is a Clinical Pharmacology information request for your response on or before COB on November 5, 2013.

- Please submit the EXCEL spreadsheet, Ethanol PG PK calculations 20May2013.xlsx and any applicable reviewer instructions.

Kindly let me know if you have any questions.

Please acknowledge your receipt of this e-mail.

Thank you

Modupe O. Fagbami
RPM
Division of Oncology Products 1
Office of Hematology and Oncology Products
CDER, FDA
10903 New Hampshire Avenue
WO-22, Room 2108
Silver Spring, Maryland 20993
Phone: 301-796-1348
Fax: 301-796-9845

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/s/

MODUPE O FAGBAMI
10/30/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

ACKNOWLEDGE –
CLASS 2 RESPONSE

Pfizer Labs
Attention: Tricia Racanelli, Pharm.D.
Director, Regulatory Affairs
World Wide Safety and Regulatory
235 East 42nd Street
New York, NY 10017

Dear Dr. Racanelli:

We acknowledge receipt on September 13, 2013, of your September 12, 2013, resubmission of your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Docetaxel Injection Concentrate, 10 mg/mL.

We consider this a complete, class 2 response to our February 14, 2013, action letter. Therefore, the user fee goal date is March 13, 2014.

If you have any questions, call me at (301) 796-1348.

Sincerely,

{See appended electronic signature page}

Modupe Fagbami
Regulatory Project Manager
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

MODUPE O FAGBAMI
10/01/2013

Cottrell, Christy L.

From: Duvall, Beth A
Sent: Wednesday, January 16, 2013 3:24 PM
To: Cottrell, Christy L.
Cc: Bertha, Amy; Raggio, Miranda; Kim, Tamy; Laughner, Erik
Subject: NDA 202356 - b2 clearance question

Hi Christy,

I've been reviewing this application today and have one question for you.

Can you confirm whether or not the protected pediatric language in the Taxotere labeling (i.e., the language protected by the M-61 exclusivity listed under NDA 20449 in the Orange Book, expires in Nov 2013) was carved out of the proposed 505(b)(2) labeling? Thanks,

Beth

Beth Duvall
Associate Director for Regulatory Affairs
CDER/Office of New Drugs
Direct Phone Number: (301) 796-0513
OND IO Phone Number: (301) 796-0700
Fax: (301) 796-9855

From: Cottrell, Christy L.
Sent: Monday, January 14, 2013 2:23 PM
To: Duvall, Beth A
Cc: Raggio, Miranda; Bertha, Amy
Subject: RE: 505(b)(2) assessment

It's actually due in a month - with the holidays, I overlooked contacting you sooner.

It's NDA 202356 for Docetaxel Injection (Pfizer, Inc.). Receipt date was August 14, 2012. PDUFA date is February 14th. We are planning another CR.

Let me know if you need anything else from me at this point. Sorry for springing it on you on such short notice.

Christy

From: Duvall, Beth A
Sent: Monday, January 14, 2013 2:19 PM
To: Cottrell, Christy L.
Cc: Raggio, Miranda; Bertha, Amy
Subject: RE: 505(b)(2) assessment

No need to send an updated assessment form, but please do reply to all on this email and let us know the specific application number and new due date so that we can be certain it's n our clearance queue. But for clarity, we do need to 'clear' it again this review cycle regardless of your planned action (CR or AP). It's the assessment form that we ask you to hold off on *archiving in DARRTS* until you're heading towards approval.

Beth

Beth Duvall
Associate Director for Regulatory Affairs
CDER/Office of New Drugs
Direct Phone Number: (301) 796-0513
OND IO Phone Number: (301) 796-0700
Fax: (301) 796-9855

From: Cottrell, Christy L.
Sent: Monday, January 14, 2013 2:14 PM
To: Duvall, Beth A
Cc: Raggio, Miranda; Bertha, Amy
Subject: RE: 505(b)(2) assessment

This is a resubmission...so no need to send an updated form again until we are ready to approve, then, right?

From: Duvall, Beth A
Sent: Monday, January 14, 2013 2:10 PM
To: Cottrell, Christy L.
Cc: Raggio, Miranda; Bertha, Amy
Subject: RE: 505(b)(2) assessment

Hi Christy,

Yes, we have to clear all 505(b)(2) applications before each and every action. If this is a RS to a previously cleared application, you don't have to send us a new/updated assessment, but they all need to be cleared. When you do send a draft assessment, please send it to our IO generic inbox 'CDER OND IO' via Outlook. Thanks,

Beth

Beth Duvall
Associate Director for Regulatory Affairs
CDER/Office of New Drugs
Direct Phone Number: (301) 796-0513
OND IO Phone Number: (301) 796-0700
Fax: (301) 796-9855

From: Cottrell, Christy L.
Sent: Monday, January 14, 2013 2:05 PM
To: Duvall, Beth A
Subject: 505(b)(2) assessment

Beth,

Do I need to do a 505(b)(2) assessment form if we are taking a CR action?

Christy

Christy Cottrell | Regulatory Project Manager | Division of Oncology Products 1, CDER, FDA
10903 New Hampshire Avenue, Room 2122 | Silver Spring, MD 20993

☎301.796.4256 (phone) ▫ 301.796.9845 (fax) | ✉ christy.cottrell@fda.hhs.gov


consider the environment before printing this e-mail

From: Cottrell, Christy L.
Sent: Wednesday, December 19, 2012 2:15 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 for Docetaxel Injection: Clarification from DMEPA on information request

Attachments: 12-19-12 Response to Pfizer Docetaxel carton questions - 12-14-12.doc

Tricia,

Please refer to your NDA 202356 for Docetaxel Injection. DMEPA has provided a clarification regarding their information request. See attached.

Feel free to contact me with any questions.

Regards,
Christy

12-19-12
ponse to Pfizer D

Christy Cottrell | Regulatory Project Manager | Division of Oncology Products 1, CDER, FDA
10903 New Hampshire Avenue, Room 2122 | Silver Spring, MD 20993
☎301.796.4256 (phone) • 301.796.9845 (fax) | ✉ christy.cottrell@fda.hhs.gov

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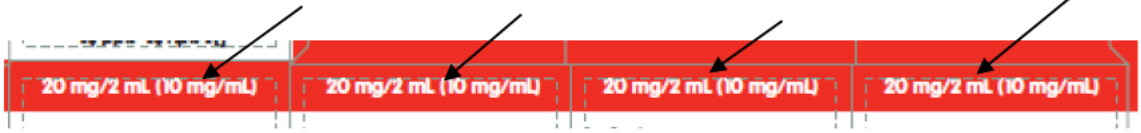
1) Request to include the concentration per mL "to the top of all panels of the carton labeling as a continuous banner to provide further emphasis on the concentration of the product."
    a. We reviewed the carton labeling for the Sandoz and Hospira marketed docetaxel products and did not find a continuous banner at the top of the panels. Please confirm how you would like this information presented or please provide a copy of a good reference source.

DMEPA has provided an example banner below.
Please note the arrows that point to the total volume and concentration per mL on the carton. When the carton is folded into a box, it forms a continuous banner at the top of the sides of the carton. DMEPA recommends a banner similar to this.



The original recommendation is provided as follows:

In red color block and in white lettering add "xx mg/xx mL (10 mg/mL)" to the top of all panels of the carton labeling as a continuous banner to provide further emphasis on the concentration of the product. The Sandoz and Hospira marketed docetaxel products are a good resource on guidance for this change. Additionally, delete the statement "((b) (4))" at the top of each carton

2) The color for the container and carton label for the Pfizer 130 mg/13 mL strength is similar to the color currently utilized for the two-vial 80 mg/2 mL product by Apotex.
    a. The Apotex carton and container labeling is not available on Daily Med or the FDA website. Would you be able to provide a copy or a link to the source so we can ensure proper color differentiation for the Pfizer product?

DMEPA is providing a sample of the color below so Pfizer can ensure proper color differentiation.

(b) (4)

(b) (4)

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/s/

CHRISTY L COTTRELL
12/19/2012

From: Cottrell, Christy L.
Sent: Monday, December 10, 2012 2:39 PM
To: 'Racanelli, Tricia'
Subject: NDA 202356 for Docetaxel Injection: Information requests

Importance: High

Tricia-

Please refer to your pending NDA 202356 for Docetaxel Injection Concentrate. See below for comments/information requests from the review team.

Microbiology

A microbiology review of NDA 202356 is in progress.

Reference is made to Section 2.10 of the draft Package Insert. We note that the PI states that '(b) (4) . However, the subsequent statement regarding chemical and physical in-use stability data for up to (b) (4) hours when stored at room temperature suggests that it may be appropriate to store the diluted product for (b) (4) at room temperature. The NDA does not contain microbiological data to support a (b) (4) post dilution period at room temperature. Further, the PI for the reference listed drug states that the final product should be used within 4 hours of dilution, including the 1 hour infusion.

- Provide microbiological data to support a post dilution holding time of (b) (4) hours at room temperature.
- In lieu of these data, modify the post dilution storage statement to be consistent with that of the referenced listed drug.
- For your convenience, we provide the following guidance for generation of a microbiological risk assessment to support your proposed extended post dilution holding period.

  The risk assessment should summarize studies that show adventitious microbial contamination does not grow under the storage conditions identified in the Package Insert. Reference is made to Guidance for Industry: ICH Q8 Pharmaceutical Development, Section II.E and Guidance for Industry: ICH Q1A(R2) Stability Testing of New Drug Substances and Products, Section 2.2.7.

  Generally, "no growth" is interpreted as not more than a 0.5 $\log_{10}$ increase from the initial count; however other evidence of growth may be significant. The test should be run at the label's recommended storage conditions, be conducted for 2 to 3-times the label's recommended storage period, and use the label-recommended fluids inoculated with

low numbers (≤100 CFU/mL) of challenge microbes. Periodic intermediate samples (which include the initial timepoint) should be obtained for enumeration of the challenge organism throughout the study. Challenge organisms may include strains described in USP <51> plus typical skin flora or species associated with hospital-borne infections.

DMEPA

Carton Labeling (1 count and 5 count)

1. Add the concentration per mL statement "10 mg/mL" just below the total drug content in all places that it appears. Highlight the "(10 mg/mL)" statement by placing it in a red color block background with "(10 mg/mL)" in white lettering to provide emphasis on the concentration of the product. Ensure the font size of the per mL concentration is smaller than the font size of the total drug content. Refer to the Unites States Pharmacopeia General Chapter <1> Injections for additional guidance, if needed.

   For example:
   White lettering with red color background

   80 mg/ 8 mL

2. In red color block and in white lettering add "xx mg/xx mL (10 mg/mL)" to the top of all panels of the carton labeling as a continuous banner to provide further emphasis on the concentration of the product. The Sandoz and Hospira marketed docetaxel products are a good resource on guidance for this change. Additionally, delete the statement "([redacted] (b) (4))" at the top of each carton.

3. Increase the font size of the following statements on the 1 count and 5 count cartons, respectively:
   "xx mL single-use vial; discard unused portion"
   "5 x xx mL single-use vials; discard unused portion"

4. With regards to the statement "Docetaxel Injection", bold "Injection" as you did on the container labels.

Carton Labeling (5 count)

1. Increase the font size of the statements on the side panels. As currently presented, the statements are all within the top half of the side panel. Utilizing large font sizes for these statements and more of the side panel will increase readability of these statements.

Container Label and Carton Labeling for the 130 mg/13 mL Product

1. Due to the availability of multiple formulations of docetaxel in varying concentrations that require different instructions for drug preparation, the potential for confusion among these products is a significant safety concern. Thus, it is essential to differentiate the labels and labeling of these products such that the potential for confusion is minimized. One important feature of the container labels and carton labeling, that may help to differentiate these products, is color. Thus, in an effort to help minimize the potential for confusion that can lead to dosing errors due to similarities or overlaps in color between the products, we take into consideration that colors should not overlap between the following:

    - One-vial vs. two-vial formulations
    - Concentration of 10 mg/mL vs. concentration of 20 mg/mL prior to dilution in infusion bag

    The color you propose for your 130 mg/13 mL strength is similar to the color currently utilized for the two-vial 80 mg/2 mL product by Apotex. Therefore, not only could the concentrations get confused but the strengths could get confused as well. This could lead to wrong dose errors. Thus, we request you choose a color for strength differentiation for your 130 mg/13 mL product that does not overlap with the currently marketed two-vial 80 mg/2 mL product by Apotex.

Please submit your responses to these information requests to the NDA as soon as possible. Feel free to contact me with any questions.

Regards,
Christy Cottrell

Christy Cottrell | Regulatory Project Manager | Division of Oncology Products 1, CDER, FDA
10903 New Hampshire Avenue, Room 2122 | Silver Spring, MD 20993
301.796.4256 (phone) ● 301.796.9845 (fax) | christy.cottrell@fda.hhs.gov

---

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/s/

CHRISTY L COTTRELL
12/10/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

INFORMATION REQUEST

Pfizer Labs
Attention: Shai Srulovich
Senior Manager Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Mr. Srulovich:

Please refer to your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Docetaxel Injection 10 mg/mL.

We also refer to your submission dated August 14, 2012. We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and requests for information.

Please submit your written response no later than **November 23, 2012**.

1. Provide compatibility data for your drug product with the proposed syringe and infusion line (e.g., polyethylene-lined administration) under the conditions described in the proposed package.

2. Propose and justify the following tests, methods, and acceptance criteria in the drug product specification, and provide an updated specification table.

   a. Osmolarity
   b. Ethanol content
   c. EDTA content

3. Provide drug product stability data for the drug product stored in upright and inverted positions. The position of the tested vial is not clearly indicated in the stability data provided in Section 3.2.P.8.3 of your NDA. A comparison of the upright and inverted position is important to determine whether contact of the drug product with the closure results in extractables from the closure components or adsorption and absorption of the drug product components into the container/closure.

4. Revise your composition of Docetaxel Injection 10 mg/mL, Table 3.2.P.1-2, Section 3.2.P .1-2 to the one presented in Table 1, Section 2.5.2.1.2 for all four presentations, where concentration of each of the components is defined. In addition, please revise the expression "(b) (4)" to "(b) (4)".

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

Sincerely,

{See appended electronic signature page}

Nallaperumal Chidambaram, Ph.D.
Branch Chief (Acting), Branch II
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

NALLAPERUM CHIDAMBARAM
11/16/2012

From: Cottrell, Christy L.
Sent: Tuesday, October 09, 2012 2:29 PM
To: 'srulee@pfizer.com'
Subject: NDA 202356 for Docetaxel Injection: Clinical information request

Importance: High

Elina,

Please refer to your pending NDA 202356 for Docetaxel Injection. I have taken over for Yolanda Adkins as project manager for this application. See below for an information request from the clinical team. Requesting response within 2 weeks.

With regards to the proposed labeling in subsections 5.8 and 5.11, Section 17, and the Patient Information that relate to new safety information due to the propylene glycol and ethanol content in this docetaxel formulation, provide a more detailed rationale that includes at least the following:

1. Estimations of the blood alcohol levels (BALs) and propylene glycol levels that will result in patients who are treated with this docetaxel product
2. A discussion of the clinical significance of the estimated BAL and propylene glycol levels
3. A discussion comparing the estimated levels to the reference listed drug product and other approved docetaxel formulations
4. A rationale that supports the additional warning labeling proposed in this resubmission
5. A discussion of any other additional actions that may be required based on the findings provided in items #1 - #4.

Feel free to contact me with any questions.

Regards,
Christy Cottrell

Christy Cottrell | Regulatory Project Manager | Division of Oncology Products 1, CDER, FDA
10903 New Hampshire Avenue, Room 2122 | Silver Spring, MD 20993
301.796.4256 (phone) ● 301.796.9845 (fax) | christy.cottrell@fda.hhs.gov


consider the environment before printing this e-mail

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/s/

CHRISTY L COTTRELL
10/09/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Mail: OSE

FROM: Frank Cross, DOP1, 301-796-0876 (New RPM to be assigned)

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
9/28/12		202356	Labeling for Resubmitted NDA 202356 505(b)(2)	8/14/13

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Docetaxel Injection Concentrate – 10 mg/mL	Class 2 Resubmission	5S 505(b)(2)	1/17/13 PDUFA Date: 2/14/13

NAME OF FIRM: Pfizer Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- X RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

ORIGINAL NDA/BLA (Class 2 resubmission)

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: **Please review the labeling provided at the attached links and provide the review team with hyour feedback. Thank you.**

EDR links to submission:

Resubmission dated 8/14/12: <\\cdsesub1\EVSPROD\NDA202356\0011>

Carton Container labeling dated 8/14/12 <\\Cdsesub1\evsprod\NDA202356\0011\m1\us>

Revised labeling 8/31/12 (PI and PPI) <\\cdsesub1\EVSPROD\NDA202356\0012\m1\us>

SIGNATURE OF REQUESTER Frank Cross, DOP1	METHOD OF DELIVERY (Check one) ☐ MAIL X DARRTS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

FRANK H CROSS
09/28/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR PATIENT LABELING REVIEW CONSULTATION

TO: **CDER-DMPP-Patient Labeling Team**

FROM: (Name/Title, Office/Division/Phone number of requestor)
Frank Cross, DOP1, 301-796-0876 (Christy Cottrell to be the RPM from 10/1/12 until PDUFA Date – 301-796-4256)

REQUEST DATE:	NDA/BLA NO.:	TYPE OF DOCUMENTS:
9/27/12	202356	Labeling for Resubmitted NDA 202356 (505(b)(2)

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE (Generally 2 Weeks after receiving substantially complete labeling)
Docetaxel Injection Concentrate – 10 mg/mL	Class 2 Resubmission	5S 505(b)(2)	1/17/13

SPONSOR:
Pfizer Laboratories, Inc.

PDUFA Date: 2/14/13

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:
(Check all that apply)
☒ PATIENT PACKAGE INSERT (PPI)
☐ MEDICATION GUIDE
☐ INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION
☒ **ORIGINAL NDA/BLA (Class 2 resubmission)**
☐ EFFICACY SUPPLEMENT
☐ SAFETY SUPPLEMENT
☐ LABELING SUPPLEMENT
☐ MANUFACTURING (CMC) SUPPLEMENT
☐ PLR CONVERSION

REASON FOR LABELING CONSULT
☒ INITIAL PROPOSED LABELING
☒ LABELING REVISION

EDR link to submission:

Resubmission dated 8/14/12: <\\cdsesub1\EVSPROD\NDA202356\0011>
Carton Container labeling dated 8/14/12 <\\Cdsesub1\evsprod\NDA202356\0011\m1\us>
Revised labeling 8/31/12 (PI and PPI) <\\cdsesub1\EVSPROD\NDA202356\0012\m1\us>

Please Note: DMPP uses substantially complete labeling, which has already been marked up by the CDER Review Team, when reviewing MedGuides, IFUs, and PPIs. Once the substantially complete labeling is received, DMPP will complete its review within 14 calendar days. Please provide a copy of the sponsor's proposed patient labeling in Word format.

COMMENTS/SPECIAL INSTRUCTIONS:
Filing/Planning Meeting: [Insert Date(s)] 9/28/12

Mid-Cycle Meeting: [Insert Date] TBD

Labeling Meetings: [Insert Dates] TBD

Wrap-Up Meeting: [Insert Date] TBD

SIGNATURE OF REQUESTER
Frank Cross, DOP1 (Christy Cottrell to be the RPM from 10/1/12 until PDUFA Date – 301-796-4256)

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)
☐ eMAIL (BLAs Only) X DARRTS

Version: 12/9/2011

Reference ID: 3196308
Reference ID: 3476209

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/s/

FRANK H CROSS
09/27/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

ACKNOWLEDGE – CLASS 2 RESPONSE

Pfizer Labs
Attention: Shai Srulovich
Senior Manager, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Srulovich:

We acknowledge receipt on August 14, 2012, of your August 14, 2012, resubmission of your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Docetaxel Injection Concentrate 10 mg/mL.

We consider this a complete, class 2 response to our February 29, 2012, action letter. Therefore, the user fee goal date is February 14, 2013.

If you have any questions, call Yolanda Adkins, Regulatory Project Manager, at (301) 796-2850.

Sincerely,

{See appended electronic signature page}

Frank H. Cross Jr., M.A., MT (ASCP)
Captain, USPHS Commissioned Corps
Chief, Project Management Staff
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

FRANK H CROSS
09/07/2012

Cross Jr, Frank H

From: Cross Jr, Frank H
Sent: Monday, August 20, 2012 5:28 PM
To: 'tricia.racanelli@Pfizer.com'
Cc: Adkins, Yolanda
Subject: RE: NDA 202356 resubmission PI

Dr. Racanelli,

Please submit revised package insert incorporating the latest RLD labeling.

Sincerely,
Frank H. Cross, Jr., MA, MT (ASCP)
Captain, USPHS Commissioned Corps
Chief, Project Management Staff
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
US Food and Drug Administration
White Oak Bldg 22, Room 2110
10903 New Hampshire Avenue
Silver Spring, MD 20993
(301) 796-0876 (office)
(301) 796-9845 (fax)
frank.crossjr@fda.hhs.gov

From: Cross Jr, Frank H
Sent: Monday, August 20, 2012 4:48 PM
To: 'tricia.racanelli@Pfizer.com'
Cc: Adkins, Yolanda
Subject: NDA 202356 resubmission

Good Afternoon, Dr. Racanelli,

We have reassigned your resubmission to Yolanda Adkins, RPM, (cc'ed on this e-mail).

Yolanda will be in touch with you as things progress.

Sincerely,
Frank H. Cross, Jr., MA, MT (ASCP)
Captain, USPHS Commissioned Corps
Chief, Project Management Staff
Division of Oncology Products 1
Office of Hematology and Oncology Products

Center for Drug Evaluation and Research
US Food and Drug Administration
White Oak Bldg 22, Room 2110
10903 New Hampshire Avenue
Silver Spring, MD 20993
(301) 796-0876 (office)
(301) 796-9845 (fax)
frank.crossjr@fda.hhs.gov

From: Kacuba, Alice
Sent: Monday, August 20, 2012 4:32 PM
To: Cross Jr, Frank H
Subject: FW: NDA 202356 resubmit.

Docetaxel resubmit.

> ---
>
> **From:** Kacuba, Alice
> **Sent:** Monday, August 20, 2012 4:31 PM
> **To:** 'Racanelli, Tricia'
> **Subject:** RE: NDA 202356 resubmit.
>
> Yes, Please send.
>
> Thank you.
> *Alice*
> Alice Kacuba, RN, MSN, RAC
> Chief, Project Management Staff
> Division of Oncology Products 1 (new name for DDOP)
> Office of Hematology and 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.
>
> > ---
> >
> > **From:** Racanelli, Tricia [mailto:tricia.racanelli@Pfizer.com]
> > **Sent:** Monday, August 20, 2012 4:20 PM
> > **To:** Kacuba, Alice
> > **Subject:** RE: NDA 202356 resubmit.
> >
> > Alice,
> >
> > In follow up to my voice message from Friday August 17, 2012 with reference to NDA 202356 (Docetaxel Injection Concentrate), we have confirmed that there are no changes to the Package Insert or PPI resulting from the submission made on August 14th, 2012. We typically would not submit the PI again unless there

have been changes as it's already available in the original eCTD submission (as a clean WORD version).

If you would still like a courtesy copy via email, please let me know.

Also, please be advised that I am the new Pfizer Regulatory liaison for Docetaxel.

Regards,

Tricia Racanelli, Pharm.D.
Director, Regulatory Strategy
WRS, Emerging Markets/Established Products
Tel: 212-733-2530
E-mail: tricia.racanelli@pfizer.com
Pfizer Medical Division
235 East 42nd Street
New York City, New York 10017

From: Kacuba, Alice [mailto:Alice.Kacuba@fda.hhs.gov]
Sent: Wednesday, August 15, 2012 7:53 PM
To: Srulevitch-Chin, Elina
Subject: NDA 202356 resubmit.
Importance: High

Hi,

Rec'd from DOP2 today. I willassign RPM thisweel. Although on quick review of the EDR submission, no package insert was submitted, only carton and container labelings.

1. Please check OB tomake sure no chnages are needed as compared to RLD
2. Resubmit package insert, PPI, etc (and include WORD versions) as an official submision to the NDA.

Thank you.
Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Oncology Products 1 (new name for DDOP)
Office of Hematology and Oncology Products
OND/CDER/FDA
301-796-1381
(f) 301-796-9845
alice.kacuba@fda.hhs.gov
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/s/

FRANK H CROSS
08/28/2012

Kacuba, Alice

From: Kacuba, Alice
Sent: Wednesday, August 15, 2012 7:53 PM
To: srulee@pfizer.com
Subject: NDA 202356 resubmit.

Importance: High

Hi,

Rec'd from DOP2 today. I willassign RPM thisweel. Although on quick review of the EDR submission, no package insert was submitted, only carton and container labelings.

1. Please check OB tomake sure no chnages are needed as compared to RLD
2. Resubmit package insert, PPI, etc (and include WORD versions) as an official submision to the NDA.

Thank you.
Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Oncology Products 1 (new name for DDOP)
Office of Hematology and Oncology Products
OND/CDER/FDA
301-796-1381
(f) 301-796-9845
alice.kacuba@fda.hhs.gov
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/s/

ALICE KACUBA
08/15/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

CMC MICRO & STERILITY ASSURANCE REVIEW REQUEST

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

E-mail to: **CDER OPS IO MICRO**

Paper mail to: **WO Bldg 51, Room 4193**

FROM: Debbie Mesmer, ONDQA PM
301.796.4023

PROJECT MANAGER *(if other than sender)*:

REQUEST DATE	IND NO.	NDA NO	TYPE OF DOCUMENT	DATE OF DOCUMENT
8/17/12		202356	Resubmission after CR-Class 2	Aug. 14, 2012

NAMES OF DRUG	PDUFA DATE	DATE TO IDENTIFY DEFICIENCIES	DESIRED COMPLETION DATE
Docetaxel Injection, 10 mg/mL	Feb. 14, 2012	November 14, 2012	To be determined

NAME OF APPLICANT OR SPONSOR:
Pfizer Labs

GENERAL PROVISIONS IN APPLICATION

- ☐ 30-DAY SAFETY REVIEW NEEDED
- ☐ NDA FILING REVIEW NEEDED BY: _____
- ☐ BUNDLED
- ☐ DOCUMENT IN EDR
- ☐ CBE-0 SUPPLEMENT
- ☐ CBE-30 SUPPLEMENT
- ☐ CHANGE IN DOSAGE, STRENGTH / POTENCY

GENERAL INSTRUCTIONS

DOCUMENT(S) TO BE REVIEWED (INCLUDE SECTION # OF NDA/IND):
Class 2 resubmission.

EDR LINK:
\\cdsesub1\EVSPROD\NDA202356\\0011

eCTD SEQUENCE NUMBER:
Global submit:

Reference ID: 3476209

COMMENTS / SPECIAL INSTRUCTIONS:

Micro Reviewer last cycle was Steven Fong. Review recommendation was approve with the following note:
1. There are no microbiology deficiencies identified.
2. Comment for CDER Only-not to be forwarded to applicant.
It is understood that DMF [redacted] (b) (4) is inactive and therefore there is no information available regarding the [redacted] (b) (4). Consequently, this reviewer understands that ONDQA will recommend an approvable decision regarding the subject NDA. From the perspective of product quality microbiology, since the [redacted] (b) (4), this reviewer does not need to review information in the currently inactive DMF ([redacted] (b) (4)), and thus is recommending approval of the subject NDA.

Indication: DOP1
DOP 1 RPM not yet assigned.

Assigned Chemistry reviewer: Josephine Jee
ONDQA PM: Debbie Mesmer

Please advise Debbie Mesmer of assigned reviewer.

SIGNATURE OF REQUESTER	REVIEW REQUEST DELIVERED BY (Check one):
Deborah Mesmer	■ DARRTS ☐ EDR ☐ E-MAIL ☐ MAIL ☐ HAND

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/s/

DEBORAH M MESMER
08/17/2012

From: Zhou, Liang
Sent: Monday, June 06, 2011 2:49 PM
To: Sickafuse, Sharon
Cc: Lambert, Tu-Van; Jee, Josephine M
Subject: FW: Overall OC Recommendation NDA 202356/000 Decision: ACCEPTABLE

FYI. Sharon.
Liang

-----Original Message-----
From: ees_admin@fda.gov [mailto:ees_admin@fda.gov]
Sent: Wednesday, June 01, 2011 5:01 PM
To: Olagbaju, Bose*; Jee, Josephine M; Zhou, Liang; Salganik, Maria*; Biswas, Sumita; Lambert, Tu-Van; Kyada, Yogesh*
Subject: Overall OC Recommendation NDA 202356/000 Decision: ACCEPTABLE

This is a system generated email message to notify you that the Overall Compliance Recommendation has been made for the above Application.

For general questions about how to use EES in your work, send an email to EESQUESTIONS (EESQUESTIONS@cder.fda.gov).
To contact the EES technical staff, send an email to CDER EES Help (EESHELP@fda.hhs.gov). Thank you.

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/s/

SHARON K SICKAFUSE
01/26/2012

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
Division of Professional Promotion

Memorandum

Date: January 25, 2012

To: File – NDA 202356

From: Carole Broadnax, Regulatory Review Officer

Subject: **Docetaxel Injection Concentrate**

OPDP acknowledges receipt of your May 11, 2011, consult request for the proposed product labeling (Package Insert (PI)) for Docetaxel Injection Concentrate, NDA 202356. OPDP notes the January 24, 2012, DOP 2 electronic mail communication that states DOP 2 plans to draft a complete response letter. Final labeling negotiations were not initiated during the current review cycle. Therefore, OPDP will provide comments regarding labeling for this application during a subsequent review cycle. OPDP requests that DOP 2 submit a new consult request during the subsequent review cycle.

If you have any questions, please contact Carole Broadnax at 301-796-0575 or Carole.Broadnax@fda.hhs.gov.

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/s/

CAROLE C BROADNAX
01/25/2012

From: Sickafuse, Sharon
Sent: Tuesday, November 29, 2011 2:54 PM
To: 'Curran, Beatrice'
Subject: NDA 202356

Hi Beatrice,

In the patent certification statement that was in the original NDA submission, Pfizer states that they intend to notify the patent holder(s) for patents 5438072 and 5698582. Please submit a signed certification that the notification did actually occur along with signed copies of the receipt of notice.

Thank you

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/s/

SHARON K SICKAFUSE
12/07/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

INFORMATION REQUEST

Pfizer Inc
US Agent for Pfizer Labs
Attention: Beatrice Curran
Associate Director, Worldwide Regulatory Affairs
235 East 42nd Street,
New York, NY 10017

Dear Ms. Curran:

Please refer to your New Drug Application (NDA) dated April 29, 2011, received April 29, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Docetaxel Injection Concentrate 10 mg/mL.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments:

1. DMF (b) (4) is inadequate to support your NDA. (See FDA information Request letter dated October 7, 2011.) The DMF is no longer active.

2. DMF (b) (4) is inadequate to support your NDA. A letter detailing the deficiencies has been sent to the DMF Holder.

3. DMF (b) (4) is inadequate to support your NDA. A letter detailing the deficiencies has been sent to the DMF Holder.

4. DMF (b) (4) is inadequate to support your NDA. A letter detailing the deficiencies has been sent to the DMF Holder.

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.
Branch Chief, Branch II
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

SARAH P MIKSINSKI
11/18/2011

NDA 202356
Docetaxel Injection Concentrate 10 mg/mL
Mid-Cycle Meeting Minutes
October 4, 2011

Review Team:
Sharon Sickafuse, RPM
Deborah Mesmer, product quality RPM
Liang Zhou, CDTL
Bill Pierce, clinical
Lillian Zhang, clin pharm
Brian Chiu, pharm/tox
Elsbeth Chikhale, biopharmaceutics
Josephine Jee, product
Steven Fong, clinical microbiology
Carole Boardnax, DPP consult
Jim Schlick, DMEPA consult
Steve Morin, DRISK consult

Indications: Treatment of breast, NSCLC, prostate, head and neck & gastric cancers.

Presentation: 20 mg/2mL, 80 mg/8mL, 130 mg/13mL and 200 mg/20mL

Package: Single vial or five-vial packs.

Upcoming Dates:

Labeling Meetings:

Carton & container: January 9
Package insert: January 10 & 23

Wrap-Up Meeting: January 24

Primary reviews due: January 25
Secondary reviews due: February 1

Send proposed labeling & PMR/PMC (if applicable) to Pfizer: February 1

CDTL review due: February 8

Action Letter: February 29, 2012

Other Issues:
Compliance evaluation is acceptable.

Order of Presentations:

A. Product – Josephine Jee

ONDQA plans to issue an IR letter with the following:

1 Batches analyses for Docetaxel Injection Concentrate were submitted for product manufactured by Pfizer (Perth) Pty Ltd. using drug substance sourced from [redacted] (b) (4). or [redacted] (b) (4). Complete Chemistry, Manufacturing and Controls information for [redacted] (b) (4) docetaxel drug substance was not provided Provide the complete CMC information or alternatively submit a statement to withdraw [redacted] (b) (4) as a drug substance manufacturer.

2. Evaluate the drug product for compounds that may leach from elastomeric or plastic components of the container closure system. Establish appropriate validated analytical procedures to identify, monitor, and quantify leached components in the drug product, and propose acceptance criteria for the levels of leached compounds in the formulation. Additionally, provide the same information for the infusion solution in the syringe, plastic bag and infusion line recommended for the intravenous infusion of Docetaxel Injection Concentrate.

3. Provide in-use compatibility and stability data for Docetaxel Injection Concentrate as prepared for infusion.

4. DMF [redacted] (b) (4) ([redacted] (b) (4)) is currently inadequate to support your NDA.

5. Revise the drug product specification to include a single set of criteria for product release and for use in stability studies. They should be based on the results of batch analyses and stability data.

Regarding the DMF issue, this DMF was [redacted] (b) (4). Pfizer can either withdraw the 20 mg and 80 mg presentations or the DMF can be resubmitted.

B. Biopharmaceutics - Elsbeth Chikhale

Biopharm does not have any issues. Pfizer's request for a waiver of the *in vivo* bioequivalence study can be granted if the clinical and pharm/tox reviewers don't have any safety concerns regarding the excipients and the percentage of the excipients in the proposed injection. The clinical and pharm/tox revewiers stated that they didn't have safety concerns.

3. Pharm/tox – Brian Chiu

Levels of impurities and specifications at expiry were above the levels specified in ICH Q3B(R2). This item will be addressed in comment #5 in the pending IR letter.

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/s/

SHARON K SICKAFUSE
10/11/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

INFORMATION REQUEST

Pfizer Inc
US Agent for Pfizer Labs
Attention: Beatrice Curran
Associate Director, Worldwide Regulatory Affairs
50 Pequot Avenue
New London, CT 06320

Dear Ms. Curran:

Please refer to your New Drug Application (NDA) dated April 29, 2011, received April 29, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Docetaxel Injection Concentrate 10 mg/mL.

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

1. Batches analyses for Docetaxel Injection were submitted for product manufactured by Pfizer (Perth) Pty Ltd. using drug substance sourced from (b) (4). or (b) (4). Complete Chemistry, Manufacturing and Controls information for (b) (4) docetaxel drug substance was not provided in NDA 202356. Provide the complete CMC information or alternatively submit a statement to withdraw (b) (4) as a drug substance manufacturer.

2. Evaluate the drug product for compounds that may leach from elastomeric or plastic components of the container closure system. Establish appropriate validated analytical procedures to identify, monitor, and quantify leached components in the drug product, and propose acceptance criteria for the levels of leached compounds in the formulation. Additionally, provide the same information for the infusion solution in the syringe, plastic bag and infusion line recommended for the intravenous infusion of docetaxel injection.

3. Provide in-use compatibility and stability data for the drug product as prepared for infusion.

4. DMF (b) (4) ((b) (4)) is currently inadequate to support your NDA. Inform your DMF holder and request that they contact Deborah Mesmer, Regulatory Project Manager for Quality, at the telephone number listed at the end of this letter.

5. Revise the drug product specification to include a single set of criteria for product release and for use in stability studies. Base this specification on the results of batch analyses, manufacturing capability, and stability data.

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
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

SARAH P MIKSINSKI
10/07/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356 **INFORMATION REQUEST**

Pfizer Labs
Attention: Beatrice Curran
Associate Director, Worldwide Regulatory Strategy
C/O Pfizer Incorporated
50 Pequot Avenue
New London, CT 06320

Dear Ms. Curran:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Docetaxel Injection Concentrate 10 mg/mL.

We also refer to your May 20, 2011 submission.

We are reviewing the Chemistry, Manufacturing and Control, Environmental Analysis section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

It appears that the API or API-precursors are synthesized/derived from a plant source. Please provide additional information on the origin of the plant source. This information is needed to determine if the NDA meets the requirements for a claim of categorical exclusion or an Environmental Assessment. Please refer to the attached document to guide you in your response.

If you have any questions, call Tu-Van Lambert, Product Quality Regulatory Health Project Manager, at (301) 796-4246.

Sincerely,

{See appended electronic signature page}

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

FDA/CENTER FOR DRUG EVALUATION AND RESEARCH

ENVIRONMENTAL ASSESSMENTS / USE OF FLORA

Source: Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications (7/1998) http://www.fda.gov/cder/guidance/index.htm#chemistry

I. NDA and ANDA APPLICATIONS

a. Cultivated Plants

Actions involving drug or biologic products derived from cultivated plants (e.g., grown in plantations, nursery stock …) are normally categorically excluded under 21 CFR 25.31(a) and/or 21 CFR 25.31(c).

i. Claims of Categorical Exclusion

To claim a categorical exclusion, the applicant must state 1) that the action requested qualifies for a categorical exclusion, citing the particular categorical exclusion that is claimed, and 2) that to the applicant's knowledge, no extraordinary circumstances exist (see 21 CFR 25.15(d)).

Typically, the following statement is provided:

> *Applicant's name* claims that approval of this (A)NDA qualifies for a categorical exclusion in accordance with 21 CFR 25.31(x) and that, to the best of the applicant's knowledge, no extraordinary circumstances exist which may significantly affect the quality of the human environment.

To facilitate Center review, when submitting a claim of categorical exclusion for actions where the drug or biologic product is derived from cultivated plants, CDER requests that the applicant provide the following information with the claim, or specifically identify where the information can be located (e.g., DMF, page number of application):

(1) biological identification (i.e., common names, synonyms, variety, species, genus and family);
(2) a statement as to whether wild or cultivated specimens are used;
(3) the geographic region (e.g., country, state, province) where the biomass is obtained; and
(4) a statement indicating:

(a) whether the species is determined under the Endangered Species Act (ESA) or the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) to be endangered or threatened,
(b) whether the species is entitled to special protection under some other Federal law or international treaty to which the United States is a party

(c) whether the species is the critical habitat of another species that has been determined to be endangered or threatened under ESA or CITES
(d) whether the species is the critical habitat of another species entitled to special protection under some other Federal law or international treaty to which the United States is a party.

CDER will use this information to evaluate whether the claim of categorical exclusion is appropriate.

b. Non-Cultivated Plants

An Environmental Assessment (EA) is ordinarily required for NDAs, abbreviated applications and applications for marketing approval of a biologic product where the drug or biologic product is *derived from plants taken from the wild*. EAs are also ordinarily required for supplements to such applications that relate to changes in the source of the wild biomass (e.g., species, geographic region where biomass is obtained), or supplements to such applications that are considered to increase the use of an active moiety or biologic substance and which will cause more harvesting than what was described in the original EA. The content and format follows.

i. EA Content and Format

This section describes the basic information that should be submitted in an EA for a drug or biologic product derived from plants taken from the wild. Alternative formats may be used, but the applicant should recognize that use of a standard format, such as described in this guidance, promotes efficiency in the review process.

1. Date

The EA should include the date the EA was originally prepared and the date(s) of any subsequent amendments.

2. Name of Applicant or Petitioner

The EA should identify the applicant who is submitting the application.

3. Address

The EA should contain the address where all correspondence is to be directed.

4. Description of Proposed Action

a. Requested Approval

The description of the requested approval should include the drug or biologic application number (if available), the drug or biologic product name, the dosage form and strength, and a brief description of the product packaging. For example, "XYZ Pharmaceuticals has filed an NDA pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRADE NAME (established name), 250 mg and 500 mg, packaged in OHDPE bottles. An EA has been submitted pursuant to 21 CFR part 25."

b. Need for Action

The EA should briefly describe the drug's or biologic's intended uses in the diagnosis, cure, mitigation, treatment, or prevention of disease.

c. Locations of Use

The EA should identify the location(s) where the product will be used. Depending on the type of product and its use, the locations of use are typically identified as hospitals, clinics and/or patients in their homes. If use is expected to be concentrated in a particular geographic region, this fact should be included.

d. Disposal Sites

Unless other disposal methods by the end user are anticipated, it is sufficient to state that at U.S. hospitals, pharmacies, or clinics, empty or partially empty packages will be disposed of according to hospital, pharmacy, or clinic procedures and/or that in the home, empty or partially empty containers will typically be disposed of by a community's solid waste management system, which may include landfills, incineration, and recycling, although minimal quantities of the unused drug could be disposed of in the sewer system.

5. Identification of Substances that are the Subject the Proposed Action

a. Nomenclature
   - i. Established Name (U.S. Adopted Name-USAN)
   - ii. Brand/Proprietary Name/Tradename
   - iii. Chemical Names or Genus/Species of Biologic Product
     - Chemical Abstracts (CA) Index Name (inverted form)
     - Systematic Chemical Name (uninverted form)

b. Chemical Abstracts Service (CAS) registration number
c. Molecular Formula
d. Molecular Weight
e. Structural (graphic) Formula/Amino Acid Sequence

6. Environmental Issues

a. Use of Resources

Information relating to the source of the plant, such as biological identification, government oversight of harvesting, geographic region where biomass is obtained, and harvesting methods

and techniques should be included in the EA. The EA should include, but not be limited to, the following types of information:

- Biological identification (i.e., common names, synonyms, variety, species, genus, and family).
- A statement as to whether wild or cultivated specimens are used.
- The geographic region (e.g., country, state, province) where biomass is obtained and whether harvesting occurred on public or private land.
- A brief description of government oversight of the harvesting including, if applicable, the identity of the authority permitting harvesting and identity of authorities consulted regarding the harvesting. Submission of copies of permits or harvesting regulations relating to the specific species is helpful. For species covered under CITES, CDER or CBER could request copies of relevant permits.
- A brief description of the applicant's oversight of the harvesting.
- A statement indicating:
    (a) whether the species is determined under the Endangered Species Act (ESA) or the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) to be endangered or threatened,
    (b) whether the species is entitled to special protection under some other Federal law or international treaty to which the United States is a party
    (c) whether the species is the critical habitat of another species that has been determined to be endangered or threatened under ESA or CITES
    (d) whether the species is the critical habitat of another species entitled to special protection under some other Federal law or international treaty to which the United States is a party.
- A statement describing the part of the plant used and whether it is a renewable resource.
- A detailed description of the method of harvest including such information as the type of harvesting (e.g., clear cut, gleaning from timber stands destined for clear cutting, salvaging, pruning), frequency of harvest, whether the harvesting technique will affect the ecosystem (and if so, how), and whether the harvesting is conducted in accordance with government regulations or guidance (include citations to applicable regulations or guidance).
- Bulk weight or other appropriate measure of biomass needed to yield one kilogram of active moiety or biologic substance, the amount that has been harvested to date to support the proposed Agency action for the product, and the amount expected to be harvested in the future.
- The amount of biomass needed to produce the active moiety or biological substance used to treat the average patient. This should be provided in terms easy to understand (e.g., 2-3 trees per patient). The expected patient population and number of kilograms of active moiety or biologic substance needed per year should be provided. ***(This information may be provided in confidential appendix).***
- An estimate of the total number of plants in the geographic region where the biomass is obtained.
- Any uses of the plant other then for the proposed use (humans, food source, habitat for fauna).

● Plant growth rates and/or life span and, if applicable, the rate of reproduction/ regeneration.
● A discussion of whether harvesting provides for sustained yield (e.g., percentage of sustainable harvest needed to supply annual needs based on the proposed use and any prior approved uses).

7. Mitigation Measures

Describe measures taken to avoid or mitigate any potential adverse environmental effects associated with the proposed action. If no adverse environmental effects have been identified, it should be so stated and indicated that no mitigation measures are needed.

Discuss mitigation measures for actions involving flora such as mitigation measures taken before (e.g., developing a process that uses a renewable part of a plant), during (e.g., limiting/selecting specimens to be harvested), and after harvesting (e.g., reforestation) (see 40 CFR 1508.20).

8. Alternatives to the Proposed Action

If no potential adverse environmental effects have been identified for the proposed action, the EA should state this. If potential adverse environmental effects have been identified for the proposed action, the EA "shall discuss any reasonable alternative course of action that offers less environmental risk or that is environmentally preferable to the proposed actions" (21 CFR 25.40(a)). The discussion should include the no-action alternative and measures that FDA or another government agency could undertake as well as those the applicant or petitioner would undertake. The EA should include a description of those alternatives that will enhance the quality of the environment and avoid some or all of the adverse environmental effects of the proposed action. The environmental benefits and risks of the proposed action and the environmental benefits and risks of each alternative should be discussed.

Discuss alternatives for actions involving flora. A discussion must be provided of the reasonable alternatives that were considered when deciding which biomass source would be used to produce the active moiety or biologic substance (21 CFR 25.40(a)). All alternatives that were considered (e.g., other species, wild or cultivated sources, chemical synthesis) should be discussed. A brief discussion of the factors (e.g., environmental effects) that were considered in deciding whether or not the alternative would be used should be provided. The no-action (i.e., no approval) alternative should also be discussed. It should be indicated if any of the alternatives not currently used are planned for use in the future.

9. Certification

{Applicant Name} confirms that it and the other parties with which it contracts for this harvesting (e.g., any and all buyers and collectors) have complied with all requirements under *{Country/State where harvested}* law to date relating to the harvesting of *{plant species}* for *{Applicant Name}*. *{Applicant Name}* commits that it will continue to comply with all requirements under *{Country/State where harvested}* law relating to such harvesting, including

any additional requirements that may be imposed in the future, and will take appropriate measures to ensure that all such other parties continue to comply as well.

10. List of Preparers

The EA should include the name, job title, and qualifications (e.g., educational degrees) of those persons preparing the assessment and should identify any persons or agencies consulted. Contract testing laboratories should be included in the list of consultants, although this may be included in a confidential appendix. Curriculum vitae can be included in lieu of a description of an individual's qualifications.

11. References

The EA should include a list of citations for all referenced material and standard test methods used in generating data in support of the EA. Copies of referenced articles that are not generally available and that are used to support specific claims in the EA document should be attached in a nonconfidential appendix.

12. Appendices

Both confidential and nonconfidential appendices can be included. A list of the appendices should be included in the EA summary document with a designation of confidential or nonconfidential following each of the listings. Typically, the nonconfidential appendices include data summary tables and copies of referenced articles that are generally unavailable or that were used to support specific claims in the EA. Proprietary or confidential information, such as use estimates and test reports, should be included in the confidential appendices.

EA FORMAT OUTLINE

1. Date
2. Name of Applicant/Petitioner
3. Address
4. Description of Proposed Action
- **a. Requested Approval**
- **b. Need for Action**
- **c. Locations of Use**
- **d. Disposal Sites**

5. Identification of Substances that are the Subject of the Proposed Action
- **a. Nomenclature**
  - **i. Established Name (U.S. Adopted Name - USAN)**
  - **ii. Brand/Proprietary Name/Tradename**
  - **iii. Chemical Names or Genus/Species of Biologic Product (e.g., virus)**
    - **●Chemical Abstracts (CA) Index Name**
    - **●Systematic Chemical Name**
- **b. Chemical Abstracts Service (CAS) Registration Number**
- **c. Molecular Formula**
- **d. Molecular Weight**
- **e. Structural (graphic) Formula/Amino Acid Sequence**

6. Environmental Issues
7. Mitigation Measures
8. Alternatives to the Proposed Action
9. List of Preparers
10. References
11. Appendices
12. Certification

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/s/

SARAH P MIKSINSKI
08/05/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

FILING COMMUNICATION

Pfizer Labs
Attention: Beatrice Curran
Associate Director, Worldwide Regulatory Strategy
C/O Pfizer Incorporated
50 Pequot Avenue
New London, CT 06320

Dear Ms. Curran:

Please refer to your New Drug Application (NDA) dated April 29, 2011, received April 29, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for "Docetaxel Injection Concentrate 10 mg/mL."

We also refer to your submissions dated May 20 and June 2, 2011.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is February 29, 2012.

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, midcycle, 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 February 1, 2012.

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

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.

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, please call Ms. Sharon Sickafuse, Senior Regulatory Health Project Manager, at (301) 796-2320.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Biologic Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

PATRICIA KEEGAN
07/06/2011

Sickafuse, Sharon

From: Suggs, Courtney
Sent: Friday, June 24, 2011 10:12 AM
To: Sickafuse, Sharon
Subject: RE: PeRC Attendance 6/29

We'll delete it.
Courtney

Courtney M. Suggs, Pharm.D., MPH
LCDR, USPHS
Regulatory Project Manager
Pediatric and Maternal Health Staff
Office of New Drugs, Immediate Office
Center for Drug Evaluation and Research
US Food and Drug Administration
10903 New Hampshire Ave.
Bldg 22, Room 6471
Silver Spring, MD 20993
Phone: (301) 796-2096
Email: courtney.suggs@fda.hhs.gov

From: Sickafuse, Sharon
Sent: Thursday, June 23, 2011 1:06 PM
To: Greeley, George
Cc: Suggs, Courtney
Subject: RE: PeRC Attendance 6/29

Ok, what, if anything, needs to be done to the Pediatric Record?

From: Greeley, George
Sent: Wednesday, June 22, 2011 2:17 PM
To: Sickafuse, Sharon
Cc: Suggs, Courtney
Subject: RE: PeRC Attendance 6/29

Hi Sharon,

The difference between two products, one being anhydrous versus the other being a trihydrate does not constitute a new active ingredient. We will remove this product from the PeRC's schedule and track this as not triggering PREA.

Thanks,
George

From: Sickafuse, Sharon
Sent: Wednesday, June 22, 2011 2:06 PM
To: Suggs, Courtney; Greeley, George
Subject: RE: PeRC Attendance 6/29

The active pharmaceutical ingredient in the Pfizer product is anhydrous docetaxel instead of the trihydrate docetaxel used in Taxotere. The Pfizer product also is a 1 vial formulation vs. the 2 vial formulation of Taxotere. The sponsor did request waiver of bioequivalence and it was granted. Perhaps this does not trigger PREA after all?

From: Suggs, Courtney

Sent: Wednesday, June 22, 2011 1:44 PM
To: Sickafuse, Sharon
Subject: RE: PeRC Attendance 6/29

Hi Sharon,

Glad that works out for everyone. By the way, I am curious what the PREA Trigger is for docetaxel? I noticed it has been submitted as a 505(b)(2). I can search and find the answer, but you probably know it off the top of your head. I notice on your paperwork for PeRC that it says this is a new active ingredient. Is this a new combination, dosage form....?

Thanks,
Courtney

Courtney M. Suggs, Pharm.D., MPH
LCDR, USPHS
Regulatory Project Manager
Pediatric and Maternal Health Staff
Office of New Drugs, Immediate Office
Center for Drug Evaluation and Research
US Food and Drug Administration
10903 New Hampshire Ave.
Bldg 22, Room 6471
Silver Spring, MD 20993
Phone: (301) 796-2096
Email: courtney.suggs@fda.hhs.gov

From: Sickafuse, Sharon
Sent: Wednesday, June 22, 2011 1:02 PM
To: Suggs, Courtney
Subject: RE: PeRC Attendance 6/29

That's good because everyone will be at the open public hearing for Avastin on the same day.

From: Suggs, Courtney
Sent: Wednesday, June 22, 2011 10:21 AM
To: Sickafuse, Sharon
Subject: PeRC Attendance 6/29

Hi Sharon,

Just wanted to let you know that the Division's attendance at PeRC on the 29th is not required.

Thanks,
Courtney

Courtney M. Suggs, Pharm.D., MPH
LCDR, USPHS
Regulatory Project Manager
Pediatric and Maternal Health Staff
Office of New Drugs, Immediate Office
Center for Drug Evaluation and Research
US Food and Drug Administration
10903 New Hampshire Ave.
Bldg 22, Room 6471
Silver Spring, MD 20993

NDA 202356
Docetaxel Injection Concentrate 10 mg/mL
Planning Meeting Agenda
May 23, 2011

Review Team:
Sharon Sickafuse, RPM
Tu-Van Lambert, product quality RPM
Bill Pierce, clinical
Lillian Zhang, clin pharm
Brian Chiu, pharm/tox
Elsbeth Chikhale, biopharmaceutics
Josephine Jee, product
Steven Fong, clinical microbiology
Carole Boardnax, DDMAC consult
Loretta Holmes, DMEPA consult

Items to be covered:

1. **Dates Milestone Letters Must Issue**:
   a. Filing Action Letter: June 28, 2011
   b. Deficiencies Identified Letter (74 day letter): July 12, 2011
   c. Action Letter: February 29, 2012

2. **Upcoming Internal Team Meetings**:
   a. Filing Meeting:scheduled for June 7, 2011
   b. Mid-Cycle Meeting: to be scheduled for end of September, Will not be scheduled during the Monday or Friday OODP timeslot.
   c. Labeling meetings TBD. DMEPA and ONDQA requested that a meeting to discuss the carton and container labeling be scheduled separate from the meeting to discuss the package insert.
   d. Wrap-up meeting to be scheduled for late January

3. Designation of CDTL: Steve Lemery (DBOP) or Sarah Pope (ONDQA)?
   Sarah Pope will be the CDTL.

4. Date of PeRC: Does the team have a preference of early vs. later? Openings are available in June and July.
   The team preferred to have the PeRC meeting sooner rather than later. Pfizer has requested a waiver of pediatric studies.

5. Review Planner – dates that reviews are due.
   Filing reviews are to be checked into DARRTS by 6-28-2011. Team members should bring letter comments, if applicable, to the filing meeting.

6. Discussion regarding biowaiver: A decision on whether to grant or deny the biowaiver must be made by the filing meeting as this is a RTF issue.

7. Tu-Van Lambert stated that she will handle the facility inspection request.

8. Would the team like to have monthly team meetings to discuss the progress of the review and identify major issues?
The team felt that a meeting every other month was fine.

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/s/

SHARON K SICKAFUSE
05/23/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202356

NDA ACKNOWLEDGMENT

Pfizer Labs
Attention: Beatrice Curran
Associate Director, Worldwide Regulatory Strategy
50 Pequot Avenue
New London, CT 06320

Dear Ms. Curren:

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: Docetaxel Injection Concentrate 10 mg/mL

Date of Application: April 29, 2011

Date of Receipt: April 29, 2011

Our Reference Number: NDA 202356

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 June 28, 2011, in accordance with 21 CFR 314.101(a).

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

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

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Biologic 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, please call Ms. Sharon Sickafuse, Senior Regulatory Health Project Manager, at (301) 796-796-2320.

Sincerely,

{See appended electronic signature page}

Karen D. Jones
Chief, Project Management Staff
Division of Biologic Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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

/s/

KAREN D JONES
05/16/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

preIND 109463

Pfizer Global Research Development
Attention: Ronald Trust, Ph.D., M.B.A.
Director
Worldwide Regulatory Strategy
50 Pequot Avenue
New London, CT 06320

Dear Dr. Trust:

Please refer to your pre-Investigational New Drug Application (pre-IND) for "Anhydrous Docetaxel 10mg/mL."

We also refer to the November 1, 2010, meeting between representatives of your firm and this agency. A copy of the official minutes of the meeting is attached for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, please call me at (301) 796-2320.

Sincerely,

{See appended electronic signature page}

Sharon Sickafuse, M.S.
Senior Regulatory Health Project Manager
Division of Biologic Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure - Meeting Minutes

MEMORANDUM OF MEETING MINUTES

MEETING DATE: **November 1, 2010**
APPLICATION: **preIND 109463**
SPONSOR: **Pfizer**
DRUG NAME: **Anhydrous docetaxel**
INDICATION: **Treatment of solid tumors**
TYPE OF MEETING: **Type B; preIND/preNDA**
MEETING RECORDER: Sharon Sickafuse

FDA ATTENDEES:
Office of Oncology Drug Products
Division of Biologic Oncology Products
Dawn Arrington, M.D.
Joseph Gootenberg, M.D.
Patricia Keegan, M.D.
Steven Lemery, M.D.
Michael Orr, Ph.D.
William Pierce, M.D.
Sharon Sickafuse, M.D.

Office of Clinical Pharmacology
Biopharmaceutics
Angelica Dorantes, Ph.D.

Division 5
Gene Williams, Ph.D.
Hong Zhao, Ph.D.

Office of New Drug Quality Assessment
Division 1
William M. Adams, Ph.D.
Liang Zhou, Ph.D.

SPONSOR ATTENDEES:
Jeffrey Alderman, Ph.D., Clinical Pharmacology
Susan Decoteau, Global CMC
Nancy Harper, Ph.D., Pharmaceutical Development
Esin Kosal, Ph.D., Global Regulatory
Angeliki Kotsianti, M.D., Ph.D., Global Medical
Rommel Lan, Ph.D., Global CMC
Ronald MacFarland, Ph.D., Drug Safety (nonclinical)
Ronald Trust, Ph.D., M.B.A., Director, Worldwide Regulatory Strategy

BACKGROUND:

On August 2, 2010, Pfizer submitted a meeting request to discuss their plans to submit a 505(b)(2) application for anhydrous docetaxel to produce a ready-to-use 10 mg/mL solution in a [redacted], medical grade polypropylene vial. The solution can be placed into an IV drip without prior dilution. Reference is made to Taxotere® 40/mL, the listed drug manufactured by Sanofi-Aventis; NDA 20-449 approved May 14, 1996. Pfizer's application will rely on FDA's findings of safety and effectiveness for Taxotere®.

In the meeting package, submitted on August 27, 2010, Pfizer proposes a single vial formulation of docetaxel injection (10 mg/mL) in four presentations of 20 mg/2 mL, 80 mg/8 mL, 130 mg/13 mL, and 200 mg/20 mL using docetaxel (anhydrous) active pharmaceutical ingredient (API). Pfizer's drug product is a clear, colorless to brown-yellow solution packaged in 2 mL, [redacted] mL and 20 mL polypropylene (medical-grade) vials closed with [redacted] ([redacted]) rubber stoppers and oversealed with [redacted] crimps and [redacted] flip-off tops. Vials are to be packaged in cartons with the prescribing information.

The proposed indications for the 505(b)(2) application are those approved for Taxotere®: breast cancer, non-small cell lung cancer, prostate cancer, gastric adenocarcinoma, and head and neck cancer.

According to the meeting package, as compared to Taxotere®, the Pfizer drug product formulation includes an identical level of docetaxel, a nearly identical level of polysorbate 80, an increased level of ethanol, and introduces [redacted], citric acid and EDTA. The meeting package states that the admixture formulation shows similar levels for each ingredient to the product formulation.

The meeting package includes a summary evaluating the risks of the excipients in the Pfizer drug product in comparison to the Taxotere® drug product based on the maximum daily dose (200 mg). Pfizer stated that local tolerance in rabbits confirmed that both Taxotere® and the Pfizer drug product at clinically relevant concentrations produced minimal vascular and perivascular irritation, as evidenced by clinical, macroscopic, and microscopic observations. Since levels of ethanol and propylene glycol in the Pfizer drug product may cause slight intoxication in humans, a precaution statement indicating that "considerations should be given to possible CNS and other effects of alcohol" will be incorporated into the prescribing information.

Pfizer conducted a comparison *in vitro* hemolytic assay. When prepared at clinically-relevant concentrations for intravenous use, minimal hemolysis was observed and there was no evidence of precipitation or blood coagulation.

Nonclinical safety studies were not conducted and are not planned.
Pfizer expects the pharmacokinetic performance of docetaxel injection 10 mg/mL in humans to be comparable to Taxotere®, and proposes to submit a justification for a biowaiver in a 505(b)(2) application.

Pfizer has commenced stability studies for docetaxel injection 10 mg/mL up to the 12 month test interval under long-term conditions specified by ICH Q1A(R2). Additionally, Pfizer has commenced stability studies for docetaxel injection 10 mg/mL up to the 6 month test interval

under accelerated conditions specified by ICH Q1A(R2). Samples of Taxotere® are also being tested under the same stability program. Pfizer stated in the meeting package that the estimated impurity levels for four specified impurities and levels of total impurities in the Pfizer drug product are expected to meet the proposed end-of-shelf life acceptance criteria.

Molecular structures of the specified impurities were provided in the meeting package (Figure 1). Pfizer extrapolated data to support the impurity qualification for reformulated drug products submitted under 505(b)(2) based on similar practice for generic applications. Reference is made to the draft Guidance for Industry, ANDAs: Impurities in Drug Products (August 2005) which indicates that the acceptance criterion for specified degradation products can be qualified by comparison to the reference product.

Pfizer provided an assessment of the safety impact of the specified impurities at the proposed acceptance criteria based on the maximum daily dose. Due to the high degree of structural similarities of impurities with docetaxel, Pfizer concluded that the proposed impurity acceptance criteria for their drug product, while higher than that observed in Taxotere®, should not impose additional safety concerns beyond those observed with docetaxel. Pfizer's review of docetaxel and the specified impurities using the DEREK system indicates no structural alerts for genotoxicity. However, docetaxel itself is a known clastogen. Therefore, given the structural similarity of the impurities to docetaxel, it is likely they will have the same clastogenic potential.

Pfizer stated that any specified impurity present in their drug product up to the end-of-shelf life limits has been adequately qualified and proposes not to conduct any additional studies to further qualify these impurities.

During product development, Pfizer qualified [redacted] (b) (4) and [redacted] (b) (4) [redacted] (b) (4) as API suppliers for use in the ICH-guided drug product registration stability program. API suppliers used to manufacture bulk solution and filled drug product batches are identified (Table 7 in the meeting package). However, for business reasons, [redacted] (b) (4) will not be included as an API supplier in the application. Proprietary information and a letter of authorization from [redacted] (b) (4) will not be provided. Despite this, Pfizer seeks to reference drug product stability data generated using [redacted] (b) (4) API as supporting studies for the stability data generated using [redacted] (b) (4) API. Each [redacted] (b) (4) and [redacted] (b) (4) API batch used in the drug product stability batches has been independently tested by Pfizer to verify compliance to the API specifications and associated compendial requirements (Table 8 in the meeting package). According to Pfizer, the data showed that API provided by [redacted] (b) (4) was comparable to API provided by [redacted] (b) (4), and the experience to date of impurity levels shows the same or lower levels in the API from [redacted] (b) (4).

Pfizer stated that drug product batches in the stability studies were all production-scale and manufactured with the same conventional commercial equipment, and thus are representative of commercial batches. Pfizer stated that the stability protocol addresses chemical, physical and microbiological test attributes including assay, impurities, subvisible particulate matter, pH, color of solution, clarity of solution, visual inspection, appearance, weight loss, bacterial endotoxins, and sterility in accordance with the ICH Q1A guidance. Additionally, Pfizer stated that drug product stability data generated to date complies with the proposed end-of-shelf life

specification (Table 9 in the meeting package). Pfizer concluded that the drug product stability data generated using API from (b) (4) and (b) (4) are supportive of the proposed shelf life for Pfizer's docetaxel injection 10 mg/mL in 2 mL, 8 mL, 13 mL and 20 mL fill volumes.

Draft FDA responses were communicated to Pfizer on October 29, 2010.

MEETING OBJECTIVES: Discuss 505(b)(2) NDA proposal

SPONSOR QUESTIONS AND FDA RESPONSES:

1. *Does the Agency concur that the in vitro and in vivo studies conducted by the Sponsor and the physicochemical characterization data to be provided will be sufficient to demonstrate similarity to the marketed Taxotere® so as to support a waiver for bioequivalence?*

   FDA Response:
   No, we do not agree. The information provided in the meeting package fails to adequately address the safety of the impurity profiles for either of the proposed drug substance suppliers, or for the proposed drug product in comparison to Taxotere®. The data presented in Table 8 do not provide a complete impurity profile for either API supplier. The data in Tables 6 and 9 do not provide a complete profile of impurities or degradants. In the NDA, provide a comparison of the impurity profiles detected at the limit of quantitation for each of the proposed API suppliers; and for both the proposed drug product and for Taxotere® at release and on stability. In addition, the proposed release and end-of shelf life specifications for API and drug product have not been established as an adequate measure of product quality.

   A waiver of the CFR requirement to provide *in vivo* bioequivalence data may be granted for your product. The information supporting the biowaiver should also include the above requested data.

   Discussion:
   FDA stated that Pfizer will need to provide complete impurity profile information for drug substance (both suppliers) and drug product with a comparison between the listed drug and proposed drug product.

   Pfizer replied that they will include this data in NDA. They will also include data on fill volume and compatibility of their product with the container closure system.

   Pfizer expressed understanding that FDA will make a decision regarding whether to grant a biowavier upon evaluation of the data provided in the NDA.

2. *Does the Agency concur that the data and conclusions regarding impurity qualification will be sufficient to enable the Agency to assess the suitability of the docetaxel product from a toxicological perspective?*

FDA Response:
Yes, provided that the impurity profiles and impurity levels in Pfizer's docetaxel injection (both drug substance and drug product) are comparable to the listed drug, Taxotere 40/mL manufactured by Sanofi-Aventis; NDA 20-449 approved May 14, 1996). If the comparison between the Pfizer docetaxel and listed drug indicate any significant differences in the impurity profiles or if any impurities exceed levels specified by the ICH Q3B (R2): Impurities in New Drug Products guidance (http://www.ich.org/LOB/media/MEDIA421.pdf), then additional nonclinical toxicology studies may be required.

Discussion:
FDA asked Pfizer to provide data and a justification in the NDA for why additional nonclinical toxicology studies should not be required for impurities that exceed levels specified by ICH Q3B (R2) (e.g., (b) (4)). This acceptability of the information will be determined at the time of NDA submission as the current data characterizing the impurity profile is immature.

3. *Does the Agency agree with the Sponsor's proposal to use drug product stability data from batches manufactured using active ingredient sourced from both* (b) (4) *and* (b) (4) *to support the proposed drug product shelf life?*

FDA Response:
Stability data for the drug product manufactured API from (b) (4) can be considered to be supportive of the shelf life for the proposed drug product, only if the profiles of the impurities and degradants observed in each drug product lot are shown to be comparable at release and over time. Please also refer to FDA's response to question #1.

In addition, it is not acceptable to observe any new degradant in the drug product manufactured with API from (b) (4) that is not observed in the drug product manufactured with API from (b) (4)

Evaluation of the overall information will take into account any information provided in the application regarding the manufacture of API from (b) (4) and the effects on the drug product-stability due to the materials of construction for the various packaging components and the headspace volumes for each fill volume.

Discussion:
Pfizer stated that they intend to provide data in the NDA to show comparability of the impurities and degradants at release and on stability between drug product manufactured with API from (b) (4) and (b) (4)

Pfizer stated that they will provide data in the NDA to confirm that there are no new degradants observed in drug product manufactured with API from (b) (4) versus (b) (4)

Pfizer stated that they will provide data in the NDA to demonstrate stability for each fill volume, as well as compatibility with the container closure system.

4. *Does the Agency wish to comment on any other aspects of the proposed plan for consideration as Pfizer progresses the development of Docetaxel Injection 10 mg/mL?*

FDA Response:
The meeting package indicates that the proposed initial expiry period is 24 months, and that 12 months of real time, room temperature data are available. Because the materials of composition for the container closure system components differ for the proposed drug product and Taxotere®, we recommend that at least 18 months of real time, room temperature stability data be provided in the NDA to support an expiry dating of 24 months. The NDA's specifications for release and shelf life testing of drug product should be the same.

Discussion:
Pfizer acknowledged FDA comments and will take them under consideration. FDA stated that because the listed drug is in a glass container and Pfizer's product is in a plastic container, Pfizer will need to provide at least 18 of months of real time stability data to support the proposed 24 month initial expiration date. Pfizer will need to provide at least 12 months of real time stability data at filing.

ADDITIONAL FDA COMMENTS:

5. FDA recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult FDA's regulations at 21 CFR 314.54, and the October 1999 Draft Guidance for Industry "Applications Covered by Section 505(b)(2)" available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079345.pdf. In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions challenging the Agency's interpretation of this statutory provision (see Docket FDA-2003-P-0274-0015, available at http://www.regulations.gov).

6. If Pfizer intends to submit a 505(b)(2) application that relies on FDA's finding of safety and/or effectiveness for one or more listed drugs, Pfizer must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). Pfizer should establish a "bridge" between the proposed drug product and each listed drug upon which Pfizer proposes to rely to demonstrate that such reliance is scientifically justified. If Pfizer intends to rely on literature or other studies for which Pfizer has no right of reference but that are necessary for approval, Pfizer also must establish that reliance on the studies described in the literature is scientifically appropriate.

If Pfizer intends to rely on the Agency's finding of safety and/or effectiveness for a listed drug (s) or published literature that describes a specific listed drug(s), Pfizer should

identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that the regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

Please be advised that circumstances could change that would render a 505(b)(2) application for this product no longer appropriate. For example, if a pharmaceutically equivalent product were approved before your application is submitted, such that your proposed product would be a duplicate of that drug and eligible for approval under section 505(j) of the act, we may refuse to file your application as a 505(b)(2) application (21 CFR 314.101(d)(9)). In such a case, the appropriate submission would be an ANDA that cites the duplicate product as the reference listed drug.

Discussion:
Pfizer asked what would happen if a 505(b)(2) was under review and during that time, an application for a pharmaceutically similar product is approved by the Agency. FDA stated that most likely, the applicant of the 505(b)2 would be requested to withdraw their application and resubmit as a 505(j), however FDA will verify this and get back to Pfizer.

Post-Meeting Addendum: FDA advises that if a duplicate drug product is approved after Pfizer submits its 505(b)(2) application, FDA may allow the application to proceed as a 505(b)(2) if it meets the regulatory criteria for approval.

OTHER DISCUSSION ITEMS:

7. Pfizer asked if a user fee or half user fee would be required. FDA stated that most likely, a half user fee would be required, however FDA will verify this and get back to Pfizer.

   Post-Meeting Addendum: FDA advises that applications for which clinical data with respect to safety or efficacy are not required for approval are generally assessed half the fee of the original application full user fee required at the time of submission.

8. Pfizer said that they attend to submit by the end of this year. If that is the case, DBOP will be the review division.

ATTACHMENT: Pfizer's Presentation

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

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

/s/

SHARON K SICKAFUSE
11/15/2010