

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
200327

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 200327

SUPPL #

HFD # 520

Trade Name Teflaro

Generic Name ceftaroline

Applicant Name Cerexa, Inc.

Approval Date, If Known October 29, 2010

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)(1)

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

YES NO

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

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

d) Did the applicant request exclusivity?

YES NO

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

5 years

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?

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA#

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

Investigation #1

YES

Explain:

!

!

! NO

! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! 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:

Title:

Date:

Name of Office/Division Director signing form:

Title:

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

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

/s/

CARMEN L DEBELLAS
10/29/2010

EDWARD M COX
10/29/2010

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # NDA 200327 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Teflaro Established/Proper Name: ceftaroline Dosage Form: Injection		Applicant: Cerexa, Inc Agent for Applicant (if applicable):
RPM: C. DeBellas		Division: Anti-Infective and Ophthalmology Products
<p>NDA's: NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>October 30, 2010</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None

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

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics ²</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 1S</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Communication Plan <input type="checkbox"/> Submitted in response to a Pediatric Written Request <input type="checkbox"/> ETASU <input type="checkbox"/> REMS not required</p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Indicate what types (if any) of information dissemination are anticipated 	<input type="checkbox"/> None <input checked="" type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input checked="" type="checkbox"/> Other Information Advisory

² Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

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

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

Yes No

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

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

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

❖ Copy of this Action Package Checklist ³	October 29, 2010
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s)
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	October 27, 2010
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	December 29, 2009
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	N/A

³ Fill in blanks with dates of reviews, letters, etc.
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❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	N/A
<ul style="list-style-type: none"> Original applicant-proposed labeling 	N/A
<ul style="list-style-type: none"> Example of class labeling, if applicable 	N/A
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> Most-recent draft labeling 	Carton- October 14, 2010 Container October 20, 2010
❖ Proprietary Name <ul style="list-style-type: none"> Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) Review(s) (<i>indicate date(s)</i>) 	Denied LTR April 7, 2010 Approval October 8, 2010 April 7, 2010 October 8, 2010
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA September 14, 2010 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC October 12, 2010 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	February 22, 2010
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> If yes, Center Director's Exception for Review memo (<i>indicate date</i>) If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> Date reviewed by PeRC <u>October 20, 2010</u> If PeRC review not necessary, explain: _____ Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
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❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)	
❖ Internal memoranda, telecons, etc.	N/A
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg October 21, 2010
• EOP2 meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg November 21, 2006
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	N/A
❖ Advisory Committee Meeting(s)	<input type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	September 7, 2010
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 29, 2010
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 29, 2010
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 28, 2010
PMR/PMC Development Templates (<i>indicate total number</i>)	<input type="checkbox"/> None 7
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	N/A
• Clinical review(s) (<i>indicate date for each review</i>)	October 29, 2010
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	See Clinical Review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management <ul style="list-style-type: none"> • REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>) • REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) • Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested Included

⁵ Filing reviews should be filed with the discipline reviews.
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Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None September 28, 2010
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 8, 2010 September 30, 2010
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 6, 2010
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 15, 2010
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 15, 2010
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None October 18, 2010
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>)	<input type="checkbox"/> None September 1, 2010 October 6, 2010
❖ Microbiology Reviews	<input type="checkbox"/> Not needed September 30, 2010
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (<i>indicate date of each review</i>)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	September 30, 2010
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁶</i>)	Date completed: August 4, 2010 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

⁶ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

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/

CARMEN L DEBELLAS
10/29/2010



NDA 200327

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Cerexa, Inc.
2100 Franklin Street, Suite 900
Oakland, California 94612

ATTENTION: Bruce Lu, RPh, RAC
Senior Director, Regulatory Affairs

Dear Mr. Lu:

Please refer to your New Drug Application (NDA) dated December 29, 2009, received December 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ceftaroline Fosamil for Injection, 400 mg and 600 mg per vial.

We also refer to your July 14, 2010, correspondence, received July 14, 2010, requesting review of your proposed proprietary name, Teflaro. We have completed our review of the proposed proprietary name, Teflaro, and have concluded that it is acceptable.

The proposed proprietary name, Teflaro, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your July 14, 2010, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Brantley Dorch, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0150. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Carmen DeBellas, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh

Director

Division of Medication Error Prevention and Analysis

Office of Surveillance and Epidemiology

Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
10/08/2010

From: [Dean, Jane](#)
To: ["Gaffagan, Steffany":](#)
Subject: NDA 200327 (Cerexa) - additional information request
Date: Wednesday, August 25, 2010 5:44:00 PM

Hi, Stephanie,

We have another information request for you.

Provide the following analyses:

1. Perform the key sensitivity analysis on Days 2, 3, 4, 5 for studies 06 & 07. Clinical failures with EOT on the day specified in the analysis are counted as non-responders. (For example, on a Day 3 analysis, clinical failures at EOT on Day 3 would be counted as non-responders, on a Day 4 analysis, clinical failures at EOT on Day 4 would be counted as non-responders, etc. Consider absence of fever as ≤ 37.6 degrees. Also perform the analyses for only changes in lesion area (ignoring absence of fever).

Repeat above for:

% reductions in lesion area from BL of $\geq 10\%$, $\geq 20\%$, $\geq 30\%$, $\geq 50\%$, $\geq 75\%$ required for responder.

Perform the above analyses separately for the following subgroups:

- Patients with and without prior antimicrobial use for any reason within 24 hrs of start of drug
- Patients with and without antipyretic use. ('Antipyretic use' defined as having antipyretic use on the day of the analysis or the day before. For example, a patient analyzed on Day 3 with anti-pyretic use on Day 3 or Day 2, a patient analyzed on Day 4 with anti-pyretic use on Day 4 or Day 3, etc.)
- Patients with and without fever at baseline
- Patients with and without concomitant anti-inflammatory use up to the Day of analysis specified above.

2. For each of the above patients subgroups and days 2,3,4,5, report and

plot the proportion of patients in each treatment group meeting an X% reduction from baseline as X is increased from 0%, 10%, 20%,....100%, for exploratory purposes.

Thanks!

Jane

Jane A. Dean, RN, MSN
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
FDA/CDER

Office: 301-796-1202

Fax: 301-796-9881

Rm. 6397, Bdg. 22

Email address: jane.dean@fda.hhs.gov

P consider the environment before printing this e-mail

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

JANE A DEAN
08/25/2010

From: [Dean, Jane](#)
To: ["SGaffagan@forestpharm.com"](mailto:SGaffagan@forestpharm.com);
Subject: NDA 200327 (cerexa) - add'l information re sensitivity analysis
Date: Thursday, August 19, 2010 5:47:46 PM

Hello, Stephanie,

I'm the PM covering for Carmen. The reviewers have asked that the following information be sent to you:

Our sensitivity analysis, as designed, only considered that all patients with cessation of spread of lesion and absence of fever at Day 3 who were clinical failures at EOT on Day 3 would be non-responders in both the key sensitivity and supporting analyses of % reduction. This analysis, being only a sensitivity analysis, did not account for the scenario in which a patient could fail to have cessation but have a substantial % reduction, such as Patient P903_06-0041-06453.

Due to such inconsistencies in cessation vs. reduction, similar sensitivity analyses were also considered in which patients could not achieve a specified % reduction without having first met the cessation requirement.

Jane

Jane A. Dean, RN, MSN
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products

Office of Antimicrobial Products

FDA/CDER

Office: 301-796-1202
Fax: 301-796-9881

Rm. 6397, Bdg. 22

Email address: jane.dean@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

JANE A DEAN
08/19/2010

Got it. I will forward to the group.

Steffany S. Gaffagan
Sr. Manager, Regulatory Affairs
Cerexa
510.285.9220 (direct)
510.285.9299 (fax)

From: DeBellas, Carmen [mailto:Carmen.DeBellas@fda.hhs.gov]
Sent: Wednesday, August 04, 2010 11:11 AM
To: Gaffagan, Steffany
Subject: Clinical Pharmacology Comment

Hi Steffany,

Please find comment below.

Clinical Pharmacology: Reference is made to Reports ICPD 00174-8 and ICPD 00174-9 submitted for NDA 200-327 on 30 Dec 2009. Verify that reported AUC₀₋₂₄ values for ceftaroline by Monte Carlo simulation using final population PK models are correct and do not reflect rather AUC for the 12-hour dosing interval or AUC₀₋₁₂.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
08/04/2010

Reference is made to your July 20, 2010 submission regarding datasets and analyses for the CABP submission. We have been examining results in the mITT Population at Day 4, and noticed several mismatches between our classifications and yours given in the datasets. This communication tries to explain some of the differences. Any clarification that would explain remaining differences would be appreciated.

In defining the mITT Population, we did not require subjects with *Klebsiella pneumoniae* to have PORT Risk Class > 2. This did not lead to any changes in Study P903-08, but in Study P903-09, we included the following mITT subjects that were not classified in your “FDAPOP2” variable as being in the population.

5009-09024
5011-09063
5015-09057
6604-09171
7004-09036

We also classified the following subjects differently for either the Day 4 clinical stability outcome (your “CSTABD4” variable) or the Day 4 symptoms outcome (your “SYMPTD4” variable).

Study P903-08:

0026-08001^b
5426-08064^c
5426-08160^d
5428-08006^b
5428-08007^d
5428-08010^d
5428-08075^d
5428-08086^a
5428-08098^c
7034-08227^a
7104-08563^a

Study P903-09:

2013-09457^a
5003-09015^{c, d}
5015-09057^a
5101-09297^a
6801-09188^a
7008-09290^a

(a) We decided to classify all subjects who had their EOT on Day 4 or earlier as failures, because none were classified as clinical cures by the investigator.

(b) We classified these subjects as having abnormal temperatures (> 37.8° C), and are unclear why you classified them as meeting the clinical stability endpoint.

(c) We classified these subjects as meeting the Day 4 symptoms endpoint, and are unclear why you did not.

(d) We classified these subjects as meeting the Day 4 clinical stability endpoint, and are unclear why you did not.

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NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
08/02/2010

FDA Response to Cerexa Communication (July 14, 2010)

cSSSI:

1. Cerexa Comment A: Clarifications requested on ‘Analysis Population for Sensitivity/Exploratory Analyses’:

Cerexa Comment A-1: Cerexa would like to confirm that the population referred to as MITT is the modified intent to treat population, consisting of all subjects who received any dose of study medication as defined in the analysis plan for the cSSSI studies.

FDA Response: We confirm that the population referred to as MITT is the modified intent to treat population.

Cerexa Comment A-2: Per discussion during our teleconference of 01Jun2010, Cerexa is providing (Attachment 1) a listing of 19 subjects admitted into the cSSSI studies due to an infected bite with an area of erythema $\geq 75 \text{ cm}^2$. Details regarding the subjects’ signs and symptoms (including severity, baseline temperature and WBC counts), area of the lesions at baseline, and pathogens are included.

Cerexa would like to confirm that the FDA agrees with the inclusion of these complicated skin infections (at least 75 cm^2) potentially associated with insect bites.

FDA Response: We agree that these patients will be included in the MITT population.

2. Cerexa Comment B: Clarifications requested ‘Key Endpoint in Sensitivity/Exploratory Analyses’: Regarding the cutoff values used in the definition of afebrile, Cerexa would like to confirm that these values refer to uncorrected temperature measured either orally, rectally or tympanically.

FDA Response: We confirm that these values refer to the uncorrected (or unadjusted temperatures measured orally, rectally, or tympanically).

3. Additional FDA Comments Regarding Key Endpoint in Sensitivity/Exploratory Analyses:

- *Subjects who met the “responder” definition (i.e. cessation of spread of lesion and absence of fever at Day 3) were evaluated as “non-responders” in the sensitivity analysis if they had an EOT Assessment at Day 3 of “clinical failure”.*
- *Subject P90306-20106561 who was assessed as “indeterminate” at EOT on Day 3 was also evaluated as a non-responder.*
- *Subjects without a Day 3 visit (or EOT visit on Day 3) were evaluated as “non-responders”.*
- *Subjects with missing measurements of lesion dimensions at Day 3 were evaluated as “non-responders”.*

- *Across both the P903-06 and P903-07 studies, 797 of 1378 patients were included in the sensitivity analyses.*
- *Patients with major abscesses with missing surrounding erythema measurements at Day 0 were excluded from the sensitivity analysis.*

CABP:

1. FDA clarification on Comment F-2:

*In order to be included in the FDA microbiological intent-to-treat population (mITT), bacterial isolates listed in **both** Section a (commonly accepted CABP pathogens) and Section b (potentially implicated CABP pathogens) obtained from sputum specimens required the presence of > 10 WBC/LPF on Gram stain of sputum to be considered pathogens.*

2. Cerexa Comment F2-5: Regarding the exclusion of subjects with *Haemophilus parainfluenzae* as the sole causative pathogen (Item 5) and as discussed during the teleconference of 01Jun2010, Cerexa has prepared a white paper (Attachment 2) supporting the inclusion of *H. parainfluenzae* as a pathogen in CABP . Cerexa would like concurrence from the agency that subjects with *H. parainfluenzae*, irrespective of whether or not present as sole causative pathogen, should be retained in the microbiological populations.

FDA Response: The Division reviewed the literature cited in the white paper and subsequently reviewed the individual subjects with appropriate sputum specimens from which H. parainfluenzae was isolated. The Division has decided to exclude H. parainfluenzae from the list of etiologies of CABP based on the following:

- *The patient characteristics (PORT Score, ongoing medical conditions, age, etc.) of the subjects were not compatible with those of patients reported in the literature whose pneumonia was attributed to H. parainfluenzae;*
- *Other bacterial pathogens were isolated from the same subject;*
- *Some subjects with a pure isolate of H. parainfluenzae only demonstrated light culture growth; and*
- *Subjects with H. parainfluenzae were identified in only 4 countries.*

The issue of Haemophilus parainfluenzae as an etiology of CABP will be discussed further in the Advisory Committee Meeting.

New Queries to Cerexa

1. Microbiology Pathogen Determination

After review of the random sample CRFs and microbiology datasets, the review team requests clarification on the following:

- a) In cSSSI Study P903-06, patient #000206462, the baseline microbiology culture yielded *Staphylococcus aureus* which was designated as “not a pathogen”. The CRF indicates that from a major abscess “bedside tissue/aspirate/pus bedside” specimen, the gram stain was positive for gram positive cocci and had 1-5 WBCs per LPF. The CRF also indicates that an isolate was obtained and two specimens were sent to the central microbiology laboratory. Based on information from the D_PMMITT dataset, it appears that both central and local microbiology laboratories identified *S. aureus* in the specimens. However, as previously stated, the dataset also indicates that this was not considered to be a pathogen and no pathogen is listed in the D_ALLMIC dataset. Please explain.

2. Provide a dataset that contains antipyretic and/or anti-inflammatory medication use and response at Day 3 for the MITT population (i.e. Lesion sizes $\geq 75 \text{ cm}^2$, Infection type of: ‘infected wounds’, ‘major abscesses’, ‘deep/extensive cellulitis’, ‘lower extremity SSSI in subjects with diabetes mellitus or PVD’, 19 patients with bite wounds, and ‘surrounding erythema $\geq 5 \text{ cm}$ (patients with major abscesses only)’).

In the dataset, include:

- Study Number
- Unique Patient ID
- Treatment Group (randomized)
- Use of concomitant medications with antipyretic activity (separate flags for Days 2 and 3)
- Use of concomitant medications with anti-inflammatory activity (NSAID, ASA, prednisone, etc.)
 - Single flag to indicate use of medications with anti-inflammatory activity during Days 1 -3
 - Duration of medication use with anti-inflammatory activity
- Separate flags for patients who have absence of fever on Day 3, cessation of spread of lesion on Day 3, and patients who had their EOT assessment performed on Day 3 and were assessed as “clinical failures”.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
07/21/2010

From: DeBellas, Carmen
Sent: Tuesday, July 20, 2010 8:57 AM
To: 'Gaffagan, Steffany'
Subject: Request
Hi,

Please find request from our Microbiology group.

Carmen.

Please communicate this comment to Cerexa Inc.

In the Phase 3 clinical trial (CABP P903-08 and P903-09 Studies), the ceftaroline MICs ranged from ≤ 0.015 $\mu\text{g/mL}$ to 0.12 $\mu\text{g/mL}$ for *Streptococcus pneumoniae*. The Agency is requesting that the MICs below 0.015 $\mu\text{g/mL}$ be provided and this data should be correlated with clinical outcome and microbiological eradication. This information is required to complete the clinical microbiology review of your NDA submission so a prompt response would be appreciated.

In the Phase 3 clinical trial (CABP P903-08 and P903-09 Studies), the ceftaroline MICs ranged from ≤ 0.015 $\mu\text{g/mL}$ to 0.03 $\mu\text{g/mL}$ for *H. influenzae* and ≤ 0.015 $\mu\text{g/mL}$ to 0.12 $\mu\text{g/mL}$ for *H. parainfluenzae*. The Agency is requesting that the MICs below 0.015 $\mu\text{g/mL}$ be provided and this data should be correlated with clinical outcome and microbiological eradication. This information is required to complete the clinical microbiology review of your NDA submission so a prompt response would be appreciated.

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/s/

CARMEN L DEBELLAS
07/21/2010

Hi Steffany,

Please find our response/requests from your email dated June 28, 2010 concerning CABP.

Carmen

Carmen DeBellas, Pharm D. RPh.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
301-796-1203

We request that for Study P903-08 and Study P903-09 you reproduce tables 10.1-2, 14.3.2.1, 14.3.2.3, and 14.3.2.10A for the newly-defined mITT Population, which show reasons for lack of evaluability, systemic antimicrobial drugs received within 96 hours of the first dose of study drug, concomitant systemic antimicrobials, and the reasons for concomitant systemic antimicrobials. Also, we request that you provide tables analogous to 14.3.2.1 showing antimicrobial drugs received within 24 hours of the first dose of study drug, instead of the first 96 hours.

We would also like to examine CRFs for mITT subjects who were classified as responders on Day 4 according to the signs and symptoms criteria, but were not classified by the investigator as clinical cures at the EOT. Please provide CRFs for these subjects. Below is the list of such CRFs we have identified that were not included in the random sample.

Study P903-08:

1004-08482

5028-08116

5127-08421

5528-08053

6633-08131

Study P903-09:

2022-09446

5003-09009

5012-09413

5204-09562

6602-09430

6602-09557

6613-09213

6618-09615

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
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/s/

CARMEN L DEBELLAS
07/02/2010

Hi Steffany,

Because we have changed our analysis endpoints and need some more specific data about individual patients for our final analysis, please send the following CRFs.

From P903-06

000806413
650606445
004106666
201206561

From P903-07

003307151
002407128
002507018
001006392
002407600
002407068
200507663
300707285
002407333
310507316
002807623
003707574
002407128
002107102

Thanks,
Carmen

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
06/28/2010

Hi Steffany,

Please find revised CABP data request- The first comment in this email is actually the last comment on the original email. I have underlined the change. The additional FDA comment is new.

Carmen

Carmen DeBellas, Pharm D. RPh.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
301-796-1203

We request that you submit new datasets for P903-08 and P903-09. Each should contain a row for each subject, a column listing the subject ID, a column flagging whether subjects are in the newly-defined microbiological intent-to-treat population, a column flagging whether subjects would be in the newly-defined microbiological intent-to-treat population if H. parainfluenzae was considered a CABP pathogen, a column flagging whether subjects meet the clinical stability endpoint on Day 3, a column flagging whether subjects meet the clinical stability endpoint on Day 4, a column flagging whether subjects meet the symptoms endpoint on Day 3, a column flagging whether subjects meet the symptoms endpoint on Day 4, a column flagging whether subjects meet both the clinical stability and symptoms endpoints on Day 3, and a column flagging whether subjects meet both the clinical stability and symptoms endpoints on Day 4.

Additional FDA comments on prior antibiotics:

We additionally request that for Study P903-08 and Study P903-09 you reproduce tables 14.3.2.1 and 14.3.2.7 for the newly-defined microbiological intent-to-treat population, which show systemic antimicrobial drugs received within 96 hours of the first dose of study drug. Also, we request that you provide similar tables showing antimicrobial drugs received within 24 hours of the first dose of study drug. As the inclusion of H. parainfluenzae as a causative CABP pathogen is under review, we request that these tables be provided with and without its inclusion.

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/s/

CARMEN L DEBELLAS
06/28/2010

Hi Steffany,

Please find information request from clinical
Carmen

The CRFs in the Application do not contain information relevant to the issues/questions we have about the following cases. Source documents from the Investigators may provide information helpful in determining association of the following deaths/SAEs leading to deaths in the following cases:

cSSSI:

Subject 5007-06358: Source documents that specify the circumstances (VS, clinical status, physician assessment, etc.) surrounding the subject's death, her immediate cause of death, and an explanation how the SAE "progression of low differentiated carcinoma of the neck" could have led to her death, would be helpful;

Subject 2106-07694: Source documents specifying the circumstances of the subject's death and her immediate cause of death (aside from the reported SAE of Bleeding of Surgically Debrided Skin Ulcer from which the subject completely recovered) would be helpful;

CABP:

Subject 2034-08238: Source documents showing ECG findings during the study (baseline, etc), vital signs, and physician assessments done preceding death, and physician assessments during and after resuscitative measures would be helpful;

Subject 5027-08585: Source documents showing actual clinical circumstances leading to the patient's death (around Day 50) (clinical status, vital signs, laboratory evaluation, medications, and therapeutic interventions) may assist in determining association;

Subject 6626-08148: Source documents showing clinical status, notes, physician assessments (including documentation of subject's alcohol dependence) around the period of deterioration leading to the subject's demise may be helpful in determining association;

Subject 8206-08236: Source documents such as baseline ECG tracings, history, and laboratory evaluation done to determine the etiology of cardiomyopathy in this subject with no prior history of cardiomyopathy may assist us in determining causation.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
06/24/2010

1. For the definition of adequate sputum specimens, please confirm that sputum specimens are acceptable irrespective of the number of squamous epithelial cells/LPF provided they contain > 10 WBC/LPF.

FDA response: We consider sputum specimens acceptable if there are ≤ 10 squamous epithelial cells/LPF and > 10 WBC/LPF.

2. Regarding Item 2b, Cerexa would like to request concurrence from the agency that the pathogens listed below can also be included as causative pathogens for CABP:

- *Enterobacter aerogenes*
- *Klebsiella pneumoniae*
- *Serratia marcescens*

FDA response: We concur that these pathogens should be included as causative pathogens for CABP. Our previous communication omitted them by mistake and we have been including patients with these pathogens in our sensitivity analyses.

3. Regarding the exclusion of subjects with *Haemophilus parainfluenzae* as the sole causative pathogen (Item 5) and as discussed during the teleconference of 01Jun2010, Cerexa has prepared a white paper (Attachment 2) supporting the inclusion of *H. parainfluenzae* as a pathogen in CABP. Cerexa would like concurrence from the agency that subjects with *H. parainfluenzae*, irrespective of whether or not present as sole causative pathogen, should be retained in the microbiological populations.

*FDA response: The white paper regarding pathogen status of *Haemophilus parainfluenzae* is under review.*

4. For the statement above stating that “Clinical stability will be assessed on Day 4, consistent with published time to stability studies in pneumonia (Halm, E.A., et al. *JAMA*, 279: 1452-1457), while requiring that stabilization be maintained for 24 hours.”, please clarify if the requirement for maintenance of stability for 24 hours implies that the criteria listed above must be met on both Days 3 and 4, rather than Day 4 only.

FDA response: The criteria must only be met at Day 4, rather than on both Days 3 and 4.

5. Please confirm that flags for Days 3 and 4 should be determined separately for each of these study days or whether a third flag should be added for subjects who met stability criteria on both Days 3 and 4.

FDA response: Flags for Days 3 and 4 should be determined separately. We requested the Day 3 flags to perform an additional sensitivity analysis for the different timepoint.

Additional FDA comments on symptoms:

Because clinical response traditionally refers to both signs and symptoms, we have decided to examine both signs and symptoms at an early timepoint in our sensitivity analysis, rather than vital signs alone. The choice of a symptoms endpoint was based on preliminary recommendations from the FNIH Biomarkers Consortium.

Specifically, we are analyzing a Day 4 endpoint based on cough, dyspnea, chest pain, and sputum production. For each of these four symptoms, we first determine at Day 4 if the symptom was worsening or improving from baseline.

For cough, dyspnea, and chest pain, this is based on the ordering Absent < Mild < Moderate < Severe of outcomes recorded on the CRFs.

We define sputum production to have been improving if it was present at baseline but was not present at Day 4, or if was present at both days but the change in character was recorded as “Improved” on the CRF. We define sputum production to have been worsening if it was not present at baseline but present at Day 4, or if it was present at both days but the change in character was recorded as “Worsened” on the CRF.

Note that a symptom can be unchanged from baseline at Day 4, in which case it is neither classified as worsening or improving.

The Day 4 symptom endpoint is then defined by classifying a subject as successful if and only if none of the four symptoms are classified as worsening, and at least one of the four symptoms is classified as improving.

Our primary sensitivity analysis will be based on ceftaroline – ceftriaxone response rates, based on classifying a subject as a responder if they meet both this Day 4 symptoms criteria and the Day 4 IDSA clinical stability criteria previously discussed.

We request that you submit new datasets for P903-08 and P903-09. Each should contain a row for each subject, a column listing the subject ID, a column flagging whether subjects are in the newly-defined microbiological intent-to-treat population, a column flagging whether subjects meet the clinical stability endpoint on Day 3, a column flagging whether subjects meet the clinical stability endpoint on Day 4, a column flagging whether subjects meet the symptoms endpoint on Day 3, a column flagging whether subjects meet the symptoms endpoint on Day 4, a column flagging whether subjects meet both the clinical stability and symptoms endpoints on Day 3, and a column flagging whether subjects meet both the clinical stability and symptoms endpoints on Day 4.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
06/24/2010

Hi Steffany,

We need some information---- CRFs, clinical or hospital notes during admission or during period preceding patient's death for the following cases:

P903-06:	Subject 5007-06358
P903-07:	Subject 2016-07561
	Subject 2106-07694
P903-08:	Subject 2031-08249
	Subject 2034-08238
	Subject 5027-08585
	Subject 6626-08148
	Subject 8206-08236

Thanks,

Carmen

Carmen DeBellas, Pharm D. RPh.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
301-796-1203

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
06/21/2010

Hi Steffany,

Please find request from our Clinical Pharmacology Reviewer:

With respect to the population PK reports 174-3 and 174-4, provide the comma separated files (SACT2.csv and CAPACT.csv) and the respective NONMEM (VI) control stream files. In addition, provide the NONMEM (VI) codes to calculate the exposure measures (e.g. AUC and Cmax) in these two population PK analyses.

Thanks,
Carmen

Carmen DeBellas, Pharm D. RPh.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
301-796-1203

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
06/08/2010

From: [Dean, Jane](#)
To: ["SGaffagan@cerexa.com"](mailto:SGaffagan@cerexa.com);
cc: [DeBellis, Carmen](#);
Subject: NDA 200327 (ceftaroline) - comments on analysis population and efficacy endpoint for cSSI and CABP
Date: Friday, June 04, 2010 3:41:37 PM

Hi, Stephanie - these are the comments that Carmen asked me to forward to you on his behalf:

cSSI

Analysis Population for Sensitivity/Exploratory Analyses: MITT patients meeting the following inclusion criteria at baseline:

- Lesion sizes $\geq 75 \text{ cm}^2$
- Infection type of: 'infected wounds', 'major abscesses', 'deep/extensive cellulitis', 'lower extremity SSSI in subjects with diabetes mellitus or PVD'
- Surrounding erythema $\geq 5 \text{ cm}$ (patients with major abscesses only)

Key Endpoint in Sensitivity/Exploratory Analyses: Percent (%) responders in above analysis population. A responder must satisfy the following:

- Cessation of spread of lesion at Day 3 ('Spread of the lesion' is defined as any increase from baseline in either the length or width measurement).
- Afebrile at Day 3 ('Afebrile' is defined using two cutoffs, one as having a highest temperature $\leq 37.6 \text{ }^\circ\text{C}$ and another as having a highest temperature $\leq 37.8 \text{ }^\circ\text{C}$)

Confirmation of Key Endpoint: To confirm the robustness of the key endpoint in the sensitivity/exploratory analyses and to account for variability due to potential measurement error, further analyses will compare treatment responder rates based on various levels of percent reduction in spread of lesion at Day 3 (e.g. 10%, 20%, 30% reduction). In these analyses, a responder must satisfy the following:

- Reduction of lesion at Day 3 ('Reduction of lesion' is defined as a decrease from baseline in the area (length times width) measurement of x%, x%=10%, 20%,30%, etc.).
- Afebrile at Day 3 ('Afebrile' is defined using two cutoffs, one as having a highest temperature $\leq 37.6 \text{ }^\circ\text{C}$ and another as having a highest temperature $\leq 37.8 \text{ }^\circ\text{C}$)

Important Secondary Endpoints Measured at EOT:

- Absolute and percent reduction from baseline in the area of lesion measurement
- Tenderness (percent absent)
- Swelling (percent absent)
- Erythema (percent absent)
- Investigator Assessment of Clinical Response (percent cures)

Note: Percent reduction from baseline at Day 3 and EOT should also be computed based on reduction in lesion length and width measurements separately

Replication: To ensure similar findings in the sensitivity/exploratory analyses, the Sponsor can submit new datasets for

P903-06 and P903-07 including new variables to flag the appropriate categorizations as outlined above. Note that there should be exactly one row per patient included in each dataset.

CABP

Analysis Population for Sensitivity/Exploratory Analysis: the Microbiological Intent-To-Treat population (mITT)

1. The mITT population consists of all subjects in the ITT population with at least one acceptable bacterial pathogen isolated from baseline microbiological culture obtained from the following sources:

- a. Blood;
- b. Pleural fluid;
- c. Broncho-alveolar lavage (BAL) specimen;
- d. Transthoracic specimen;
- e. Deep tracheal specimen; and
- f. Adequate sputum specimen. An adequate sputum specimen is defined as a sputum sample with > 10 WBCs/low-power field.

Subjects with a positive urinary antigen test for *Streptococcus pneumoniae* are also included in the mITT population.

2. The following bacteria are determined to be acceptable as etiologic CABP pathogens:

a. Commonly accepted CABP Pathogens:

1. *Streptococcus pneumoniae*
2. *Haemophilus influenzae*
3. *Moraxella catarrhalis*
4. *Staphylococcus aureus*
5. *Streptococcus pyogenes*.

b. The following potentially implicated CABP pathogens (enteric Gram negative rods) will be considered acceptable as etiologic cause of CABP only if subjects are classified as PORT III or above and there are > 10 WBC/LPF seen on Gram stain if the source of the specimen is sputum:

1. *Citrobacter freundii complex*
2. *Citrobacter koseri*
3. *Enterobacter cloacae*
4. *Escherichia coli*

5. *Klebsiella oxytoca*

6. *Proteus mirabilis*
7. *Serratia liquefaciens*.

3. If one of the pathogens listed above is present, and

Legionella pneumophila is present as a co-

pathogen, the subject is included in the mITT population.

4. If one of the pathogens listed above is present, and either *Mycoplasma pneumoniae* or *Chlamydomphila pneumoniae* are present as a co-pathogen, the subject is included in the mITT population.
5. Subjects with *Haemophilus parainfluenzae*, but no other pathogens listed above, should not be included.

Early Clinical Stability Endpoints used for Sensitivity Analysis

For sensitivity analysis, the Agency defines a patient to have reached clinical stability by Day 4 if they meet the following criteria:

- o Temperature ≤ 37.8 degrees Celsius. This refers to uncorrected temperature, measured orally, rectally, or tympanically.
- o Heart rate ≤ 100 beats per minute.
- o Respiratory rate ≤ 24 breaths per minute.
- o Systolic blood pressure ≥ 90 mm Hg.
- o Oxygen saturation $\geq 90\%$.
- o Confusion/disorientation is absent.

These criteria are based on a “clinical stability” definition from 2007 consensus treatment guidelines of the Infectious Diseases Society of America and American Thoracic Society (*Clinical Infectious Diseases*, 44:S27-72).

Clinical stability will be assessed on Day 4, consistent with published time to stability studies in pneumonia (Halm, E. A., et. al. *JAMA*, 279: 1452-1457), while requiring that stabilization be maintained for 24 hours.

Note that the IDSA/ATS definition also refers to “ability to maintain oral intake,” but we did not include this component as it is not captured in the case report forms.

If the data needed to determine stability according to this definition are incomplete or missing, we score the subject as having not reached stability.

When analyzing this endpoint in different analysis populations, we do not require any of the vital sign components to be abnormal at baseline.

Replication

To ensure that we are analyzing the same sensitivity population and the same endpoint, it would be helpful to initially submit new datasets for P903-08 and P903-09. Each should contain a row for each subject, and four columns: a column listing the subject ID, a column flagging whether subjects are in the newly-defined microbiological intent-to-treat population, a column flagging whether subjects are classified as clinically stable on Day 3 according to the above criteria, and a column flagging whether subjects are classified as clinically stable on Day 4. Requests for analyses will be forthcoming.

Sincerely,

Jane A. Dean

Jane A. Dean, RN, MSN

Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
FDA/CDER

Office: 301-796-1202

Fax: 301-796-9881

Rm. 6397, Bdg. 22

Email address: jane.dean@fda.hhs.gov

P consider the environment before printing this e-mail

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

JANE A DEAN
06/04/2010

Hi Steffany,

I have a request from our reviewers for some CRF's.

We need some CRFs of certain subjects with missing data on Day 4 which were not included in the random sample of CRFs submitted by the Sponsor. Please request the CRFs for the following:

Study 08:
5039-08548
5428-08003
6131-08060
6629-08058

Study 09:
2012-09565
6513-09475
6604-09185
6801-09188

Thanks,

Carmen

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
05/27/2010

Hi Steffany,

Please find information request below:

The tabulation (raw data) and analysis data sets for ceftaroline do not contain a unique patient identifier that can be used with all datasets.

Please ask Cerexa to resubmit all datasets for NDA 200327. They need to include a unique patient identifier for each patient, that can be used across all data sets (tabulation and analysis). We need this done to be able to use our review tools. Please ask them for a timeframe for turn around.

Thanks,

Carmen

Carmen DeBellas, Pharm D. RPh.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
301-796-1203

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
05/18/2010



NDA 200,327

INFORMATION REQUEST

Cerexa, Inc.
Attention: Bruce Lu, R.Ph., RAC
Senior Director, Regulatory Affairs
2100 Franklin St., Suite 900
Oakland, CA 94612

Dear Mr. Lu:

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

We are reviewing the Chemistry, Manufacturing and Controls sections 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. Please provide a table linking the proposed acceptance criteria for all listed impurities and degradation products in Table 3.2.P.5.4.2-1 (Batch Analysis for the NDA Registration Batches of Ceftaroline fosamil for Injection) to their qualification levels.
2. Please provide the chemical structure and molecular weight for ceftaroline fosamil monoacetate hydrate, the prodrug. Please also provide the structure and molecular weight of ceftoroline.
3. Please clarify whether any chemical change [REDACTED] (b) (4) or physical change [REDACTED] (b) (4) occurs when the drug substance [REDACTED] (b) (4) the arginine.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Carmen DeBellas, Regulatory Project Manager the Office of New Drugs (Carmen.DeBellas@fda.hhs.gov).

If you have any questions regarding this letter, call Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Acting Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

STEPHEN P MILLER
04/23/2010

From: Gaffagan, Steffany [SGaffagan@cerexa.com]
Sent: Tuesday, April 20, 2010 12:24 PM
To: DeBellas, Carmen
Subject: RE: Clinical Pharmacology Information request

Attachments: emfalert.txt
Thank you,

I will forward to the group.

Steffany S. Gaffagan
Sr. Manager, Regulatory Affairs
Cerexa
510.285.9220 (direct)
510.285.9299 (fax)

From: DeBellas, Carmen [mailto:Carmen.DeBellas@fda.hhs.gov]
Sent: Tuesday, April 20, 2010 9:22 AM
To: Gaffagan, Steffany
Subject: Clinical Pharmacology Information request

Hi Steffany,

Please find information request from clinical pharmacology. Carmen

Clinical Pharmacology: Reference is made to the submission of NDA 200-327 on 30 Dec 2009 for ceftaroline fosamil, in which the study report (dated Mar 2009), bioanalytical study report (PRD-RPT-BDM-00120, dated Oct 2008), and method validation reports (PRD-RPT-BDM-00077, dated Sep 2008 and PRD-RPT-BDM-00080, dated Sep 2008) for the mass balance study, Study 903-13, were provided. It appears the dilution integrity of bioanalytical methods were investigated for a 1:10 dilution in plasma (PRD-RPT-BDM-00077) and a 1:5 dilution in urine (PRD-RPT-BDM-00080). However, ceftaroline concentrations in urine (for 0-2, 2-4, and 4-8 hour collection periods) exceed the standard curve range (0.5-50 µg/mL) even after a 1:5 dilution. Provide the necessary bioanalytical validation data to ensure that analyzed ceftaroline urine concentrations in Study 903-13 did not exceed the upper limit of the standard curve range and can be accurately quantitated after appropriate dilution of the urine sample.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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CARMEN L DEBELLAS
04/20/2010

From: Gaffagan, Steffany [SGaffagan@cerexa.com]
Sent: Monday, April 12, 2010 1:50 PM
To: DeBellas, Carmen
Subject: RE: Clinical Pharmacology Comment

Attachments: emfalert.txt
Thanks Carmen,

I will forward to my group.

Steffany S. Gaffagan
Sr. Manager, Regulatory Affairs
Cerexa
510.285.9220 (direct)
510.285.9299 (fax)

From: DeBellas, Carmen [mailto:Carmen.DeBellas@fda.hhs.gov]
Sent: Monday, April 12, 2010 10:29 AM
To: Gaffagan, Steffany
Subject: Clinical Pharmacology Comment

Hi Steffany,

Please find clinical pharmacology comment below:

Carmen

Carmen DeBellas, Pharm D. RPh.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
301-796-1203

Clinical Pharmacology: Reference is made to the submission of NDA 200-327 on 30 Dec 2009 for ceftaroline fosamil for injection. In the Bioanalytical Report for Study P903-01 (Report # MC04169, dated 15 Sep 2008), it was indicated that a shipment of samples received on 24 May 2004 (consisting of 277 plasma samples and 133 urine samples) were thawed on arrival. See the following comments:

1. Identify which samples were received thawed on 24 May 2004. This includes subject number, specimen sample (e.g., plasma), and pharmacokinetic time point (e.g., 1 hour after end of infusion).
2. Provide details on how these thawed samples were verified to ensure that reported results were accurate. There does not appear to be any room temperature stability information for the bioanalytical methods used in

Study P903-01 that would indicate thawing would not compromise the integrity of the samples.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
04/12/2010



NDA 200327

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

Cerexa, Inc.
2100 Franklin Street, Suite 900
Oakland, California 94612

ATTENTION: Bruce Lu, RPh, RAC
Senior Director, Regulatory Affairs

Dear Mr. Lu:

Please refer to your New Drug Application (NDA) dated December 29, 2009, received December 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ceftaroline Fosamil for Injection, 400 mg and 600 mg per vial.

We also refer to your January 8, 2010, correspondence, received January 8, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

The proposed proprietary name (b) (4) is orthographically similar to and shares overlapping product characteristics with the product (b) (4)

(b) (4)

(b) (4)

(b) (4)

In addition to the orthographic appearance, these products share overlapping characteristics (b) (4)

(b) (4)

We recognize that our conclusion on the similarity of this name pair differs from your external evaluation conducted by the (b) (4) concluded that (b) (4)

(b) (4)

(b) (4)



We note that you have proposed an alternate proprietary name in your submission dated January 8, 2010. In order to initiate the review of the alternate proprietary name, (b) (4) submit a new complete request for proprietary name review. The review of this alternate name will not be initiated until the new submission is received.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Brantley Dorch, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0150. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Carmen DeBellas, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

DENISE P TOYER on behalf of CAROL A HOLQUIST
04/07/2010



FILING COMMUNICATION

NDA 200327

Cerexa, Inc.
Attention: Bruce Lu, R.Ph., RAC
Senior Director, Regulatory Affairs
2100 Franklin Street, Suite 900
Oakland, CA 94612

Dear Mr. Lu:

Please refer to your new drug application (NDA) dated December 30, 2009, received December 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (ceftaroline fosamil for injection).

We have completed our filing review and have determined that your application was sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application was 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 October 30, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, 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 October 2, 2010.

During our filing review of your application, the application did not appear to provide information on drug product stability/impurity profile and any new impurities formed due to the (b) (4). If this information has already been included please provide the exact location in the NDA. Note that the applicability of the (b) (4) used during drug product manufacture is unclear.

We are providing the preceding comments to give you preliminary notice of a potential review issue. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Please respond only to the preceding request for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

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 indications in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full deferral of pediatric studies for this application. Once we have reviewed your request, we will notify you of our decision.

If you have any questions, call Carmen DeBellas, R.Ph, PharmD, Regulatory Project Manager, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

Katherine A. Laessig, MD
Deputy Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

KATHERINE A LAESSIG
03/26/2010



NDA 200,327

INFORMATION REQUEST

Cerexa, Inc.
Attention: Bruce Lu, R.Ph., RAC
Senior Director, Regulatory Affairs
2100 Franklin St., Suite 900
Oakland, CA 94612

Dear Mr. Lu:

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

We are reviewing the Chemistry, Manufacturing and Controls sections 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. FDA concurs that (b) (4) are the starting materials for the drug substance.
2. FDA asked during the pre-NDA meeting whether (b) (4) Please explain any (b) (4) steps that you have taken to address this issue. FDA did not agree that final testing is adequate.
3. Limited stability data are provided for the 400 mg strength. Will you be updating with additional stability for the 400 mg strength during the review cycle? What are the differences in head space between the two configurations?
4. DMF# (b) (4) Type: III refers to (b) (4). The reviewer found that there are multiple products referred to as (b) (4) in the DMF. Please provide the product number and a description of the (b) (4) in the NDA.

To facilitate prompt review of your response, please also provide an electronic courtesy copy of your response to both Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (Jeannie.David@fda.hhs.gov), and Carmen DeBellas, Regulatory Project Manager the Office of New Drugs (Carmen.DeBellas@fda.hhs.gov).

If you have any questions regarding this letter, call Jeannie David, Regulatory Project Manager, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Stephen P. Miller, Ph.D.
Acting Chief, Branch IV
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

STEPHEN P MILLER
03/25/2010

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

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

TO: CDER-DDMAC-RPM	FROM: (Name/Title, Office/Division/Phone number of requestor) Division of Anti-Infective and Ophthalmology Products Carmen DeBellas, Project Manager
------------------------------	--

REQUEST DATE 2.24.10	IND NO.	NDA/BLA NO. 200327	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW) Labeling for New NDA
-------------------------	---------	-----------------------	---

NAME OF DRUG (b) (4) (ceftaroline)	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG 1S	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting) 9/15/10
--	------------------------------------	------------------------------	---

NAME OF FIRM: Cerexa	PDUFA Date: 10/29/10
-------------------------	----------------------

TYPE OF LABEL TO REVIEW

TYPE OF LABELING: (Check all that apply)	TYPE OF APPLICATION/SUBMISSION	REASON FOR LABELING CONSULT
<input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE(IFU)	<input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	<input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION

EDR link to submission:
\\CDSESUB1\EVSPROD\NDA200327

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

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: May 21, 2010
Labeling Meetings: TBA
Wrap-Up Meeting: TBA

SIGNATURE OF REQUESTER
Carmen DeBellas

SIGNATURE OF RECEIVER	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> eMAIL <input type="checkbox"/> HAND
-----------------------	---

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
02/24/2010

REQUEST FOR CONSULTATION

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

FROM: **Andrew Yu, Review Chemist (ONDQA) 301-796-1488**
and Jeannie David, Project Manager (ONDQA) 301-796-4247

DATE 2/10/10	IND NO.	NDA NO. 200-327	TYPE OF DOCUMENT NDA original submission	DATE OF DOCUMENT 12/30/09
NAME OF DRUG Ceftaroline fosamil for Injection		PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG Antibiotic (NME)	DESIRED COMPLETION DATE August 1, 2010

NAME OF FIRM:
Cerexa Inc

REASON FOR REQUEST

I. GENERAL

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

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 BIOAVAILABILITY 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 RICK ANALYSIS
--	--

V. SCIENTIFIC INVESTIGATIONS

CLINICAL	PRECLINICAL
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COMMENTS/SPECIAL INSTRUCTIONS:

Microbiology consult for Sterile injection:

1. Sterile manufacturing of NDA 200,327.
2. Sterile manufacturing of Ceftaroline fosamil drug substance - DMF 23167 (Vol 1.3) *
3. (b) (4)
4. (b) (4)

- * Volume with review – copy can be sent at request.
- Other DMF volumes are in DMF Document room.
- NDA 200,327 is in EDR : <http://darrts.fda.gov:7778/darrts/viewEDR.do?suppDocId=7087819>

SIGNATURE OF REQUESTER Jeannie David {see electronic signature} on behalf of Andy Yu	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> MAIL
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200327	----- ORIG-1	----- CEREXA INC	----- ceftaroline fosamil for injection

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/s/

JEANNIE C DAVID
02/10/2010

REQUEST FOR CONSULTATION

TO (Office/Division): **Interdisciplinary Review Team for QT**

FROM (Name, Office/Division, and Phone Number of Requestor): **Division of Anti-Infective and Ophthalmology Products - Carmen DeBellas -Project Manager & Dr. Ariel Procalla Medical Officer**

DATE
February 3, 2010

IND NO.

NDA NO.
200327

TYPE OF DOCUMENT
New Drug Application

DATE OF DOCUMENT
December 31, 2009

NAME OF DRUG
(b) (4) (ceftaroline fosamil)

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG
1S

DESIRED COMPLETION DATE
August 1, 2010

NAME OF FIRM: **Cerexa Inc.**

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG SAFETY

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

V. SCIENTIFIC INVESTIGATIONS

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

COMMENTS / SPECIAL INSTRUCTIONS: **Please review QT studies submitted with this NDA located in the EDR under NDA 200327**

SIGNATURE OF REQUESTOR
Carmen DeBellas

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
02/03/2010



NDA 200327

NDA ACKNOWLEDGMENT

Cerexa, Inc.
Attention: Bruce Lu, R.Ph., RAC
Senior Director, Regulatory Affairs
2100 Franklin St., Suite 900
Oakland, CA 94612

Dear Mr. Lu:

We have received your new drug application (NDA) submitted 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: (b) (4) (ceftaroline fosamil for injection)

Date of Application: December 30, 2009

Date of Receipt: December 30, 2009

Our Reference Number: NDA 200327

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 28, 2010 in accordance with 21 CFR 314.101(a).

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

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

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

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

If you have any questions, call Carmen DeBellas, Regulatory Project Manager, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

Carmen DeBellas, R.Ph., Pharm D.
Project Manager
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200327	ORIG-1	CEREXA INC	ceftaroline fosamil for injection

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/s/

CARMEN L DEBELLAS
01/11/2010