

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207131Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 207131

SUPPL #

HFD #

Trade Name Cefazolin Injection 2 g/100 mL

Generic Name Cefazolin

Applicant Name Celerity Pharmaceuticals, LLC

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES NO

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

505(b)(2)

b) 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.

This submission is for a dosage form that is currently approved. It did not require clinical data or bioequivalence studies. The Sponsor was granted a waiver for in vivo bioavailability/bioequivalence studies.

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:

c) Did the applicant request exclusivity?

YES NO

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

d) 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# 050779

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

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

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

YES NO

If yes, explain:

=====

Name of person completing form: Fariba Izadi, PharmD
Title: Senior Regulatory Health Project Manager
Date: 08-03-15

Name of Office/Division Director signing form: Sumathi Nambiar, MD, MPH
Title: Director, Division of Anti-Infective Products

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

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

/s/

FARIBA IZADI
08/07/2015

SUMATHI NAMBIAR
08/07/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 207131 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Cefazolin Injection, USP Established/Proper Name: Cefazolin Injection, USP Dosage Form: 2 g/100 mL		Applicant: Celerity Pharmaceuticals, LLC. Agent for Applicant (if applicable): N/A
RPM: Fariba Izadi		Division: Anti-Infective Products
NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)	<p><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></p> <ul style="list-style-type: none"> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) <p><input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>) Date of check:</p> <p><i>Note: 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.</i></p>	
❖ Actions		
<ul style="list-style-type: none"> Proposed action User Fee Goal Date is <u>08-16-2015</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
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		<input type="checkbox"/> Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

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

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority: Standard Priority
 Chemical classification (new NDAs only):
 (*confirm chemical classification at time of approval*)

- | | |
|---|---|
| <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 |
| <input type="checkbox"/> Breakthrough Therapy designation | |

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

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

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

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

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	Not submitted Paragraph (1) <input type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
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) Ack 10-30-14 No filing Issues 12-16-14 Approval
Labeling	
❖ Package Insert <i>(write submission/communication date at upper right of first page of PI)</i>	
• Most recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i>	<input checked="" type="checkbox"/> Included
• Original applicant-proposed labeling	<input checked="" type="checkbox"/> Included
❖ 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 type="checkbox"/> None
• Most-recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i>	<input type="checkbox"/> Included
• Original applicant-proposed labeling	<input type="checkbox"/> Included
❖ Labels (full color carton and immediate-container labels) <i>(write submission/communication date on upper right of first page of each submission)</i>	
• Most-recent draft labeling	<input checked="" type="checkbox"/> Included
❖ Proprietary Name	NA
• Acceptability/non-acceptability letter(s) <i>(indicate date(s))</i>	
• Review(s) <i>(indicate date(s))</i>	
❖ Labeling reviews <i>(indicate dates of reviews)</i>	RPM: <input checked="" type="checkbox"/> DMEPA: <input checked="" type="checkbox"/> 05-06 & 6-11-15 DMPP/PLT (DRISK): <input checked="" type="checkbox"/> None OPDP: <input checked="" type="checkbox"/> 06-30-15 SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> None Product Quality <input checked="" type="checkbox"/> included in CMC Review Other: <input checked="" type="checkbox"/> None
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting <i>(indicate date of each review)</i>	03-17-15
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	06-11-15
❖ 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	
• Applicant is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

<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 _____ If PeRC review not necessary, explain: _____ 	This application does not trigger PREA.
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>)	Included
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	NA
❖ Minutes of Meetings	
<ul style="list-style-type: none"> • If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) 	N/A or no mtg
<ul style="list-style-type: none"> • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> May 30, 2014
<ul style="list-style-type: none"> • EOP2 meeting (<i>indicate date of mtg</i>) 	No mtg
<ul style="list-style-type: none"> • Mid-cycle Communication (<i>indicate date of mtg</i>) 	N/A
<ul style="list-style-type: none"> • Late-cycle Meeting (<i>indicate date of mtg</i>) 	N/A
<ul style="list-style-type: none"> • Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (<i>indicate dates of mtgs</i>) 	N/A
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> • Date(s) of Meeting(s) 	N/A
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	None
Division Director Summary Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 08-07-15
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 08-07-15
PMR/PMC Development Templates (<i>indicate total number</i>)	None
Clinical	
❖ Clinical Reviews	
<ul style="list-style-type: none"> • Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> No separate review
<ul style="list-style-type: none"> • Clinical review(s) (<i>indicate date for each review</i>) 	07-06-15, 07-17-15
<ul style="list-style-type: none"> • 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>)	No Clinical studies needed
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	N/A

❖ Risk Management	
<ul style="list-style-type: none"> REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	N/A N/A None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 07-20-15
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review 07-17-15
Statistical Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/>
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 07-17-15
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
<ul style="list-style-type: none"> ADP/T Review(s) (<i>indicate date for each review</i>) Supervisory Review(s) (<i>indicate date for each review</i>) Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>) 	<input type="checkbox"/> No separate review <input checked="" type="checkbox"/> No separate review <input checked="" type="checkbox"/> 12-08-14
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
<ul style="list-style-type: none"> Tertiary review (<i>indicate date for each review</i>) Secondary review (e.g., Branch Chief) (<i>indicate date for each review</i>) Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None <input checked="" type="checkbox"/> None 06-17-15 07-29-15
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Quality Micro 06-29-15 Biopharmaceutics 06-05-15

❖ 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>)	June 17, 2015
<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"/> Facilities inspections (<i>action must be taken prior to the re-evaluation date</i>) (<i>only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)</i>)	<input checked="" type="checkbox"/> Acceptable Re-evaluation date: <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) 	<input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>Notify CDER OND IO</i>)
<ul style="list-style-type: none"> • Finalize 505(b)(2) assessment 	<input checked="" type="checkbox"/> Done
❖ For Breakthrough Therapy (BT) Designated drugs: <ul style="list-style-type: none"> • Notify the CDER BT Program Manager 	N/A (<i>Send email to CDER OND IO</i>)
❖ For products that need to be added to the flush list (generally opioids): Flush List <ul style="list-style-type: none"> • Notify the Division of Online Communications, Office of Communications 	N/A
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	N/A
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	N/A
❖ Ensure Pediatric Record is accurate	N/A
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

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

/s/

FARIBA IZADI
08/10/2015

Izadi, Fariba

From: Izadi, Fariba
Sent: Wednesday, June 24, 2015 5:10 PM
To: byurschak@celeritypharma.com
Cc: Amber Sheriff
Subject: 207131-Cefazolin injection- Package Insert-first draft
Attachments: 207131 pi-draft-labeling-text-Clean copy).docx; 207131 pi-draft-labeling-text-original-draft-v3.docx

Importance: High

Dear Brent,

Attached, Please find a copy of our proposed changes to the package insert for NDA 207131, Cefazolin injection. For your convenience, I have included a clean copy and a marked up version of the label. Please do not hesitate to contact me if you need further assistance.

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

Please confirm receipt of this email

11 Page(s) of Draft Labeling have been Withheld in Full
as b4 (CCI/TS) immediately following this page

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

/s/

FARIBA IZADI
06/25/2015

From: Izadi, Fariba
Sent: 6/19/2015 9:50:09 AM
To: 'byurschak@celeritypharma.com'
Subject: NDA 207131-cefazolin-Response to information request
Importance: High

Dear Brent,

We have reviewed your submission dated June 11, 2015 responding to our May 29th, 2015 information requests regarding the carton and container label and have found your proposal and revisions acceptable. Please submit your revised carton and container labeling officially to the NDA.

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

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

/s/

FARIBA IZADI
06/25/2015

From: Izadi, Fariba
Sent: 5/29/2015 12:10:02 PM
To: byurschak@celeritypharma.com
Subject: NDA 207131-Cefazolin-Additional recommendations
Importance: High

Dear Brent,

We are reviewing your NDA application dated October 16, 2014 for (Cefazolin (2 g/100 mL) in 4% Dextrose in Galaxy Plastic Container) and have the following recommendations.

1. Revise the statement “Each 100 ml contains...” to include the excipient “water for injection, USP”.
2. Revise the statement “(b) (4)” to read “single use only – discard unused portions”
3. Revise the caution statement to read (b) (4)

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

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/s/

FARIBA IZADI
05/29/2015

From: Izadi, Fariba
Sent: 5/8/2015 3:03:06 PM
To: 'Brent Yurschak'
Subject: NDA 207131-Cefazolin-Information request
Importance: High

Dear Brent,

We are reviewing your NDA application dated October 16, 2014 for (Cefazolin (2 g/100 mL) in 4% Dextrose in Galaxy Plastic Container) and have the following recommendations.

A. Container Label

1. Revise the font color to another color other than (b) (4) to distinguish Cefazolin (2 g/100 mL) in 4% Dextrose in Galaxy Plastic Container (b) (4)
2. To increase the prominence of the product name and strength on the principal display panel, consider decreasing the size of the “Celerity Pharmaceuticals, LLC” logo that competes with more important information on the label.
3. To prevent misinterpretation of the Celerity logo as the product name, we recommend relocating “Celerity Pharmaceuticals, LLC” logo from line 1 to appear under the bottom of the principal display panel (similar to the referenced RLD container).
4. Revise the NDC numbers so that the carton labeling and bag label NDC numbers are different for these two package configurations.
5. Relocate the fill volume statement “100 ml” to appear next to the 2g so that the total quantity per total volume are represented in the strength statement for clarity and prominence of this important information similar to the referenced RLD container as follows: **2 g per 100 ml.**
6. Revise the statement (b) (4) read “For Intravenous Infusion Only” (b) (4)
7. The proposed labels do not indicate where the lot number and expiration date will appear. Per 21CFR 201.17 and 21CFR 201.18, please indicate where the required lot number and expiration date will appear on the labels (or if the lot and expiration will be embossed on the bag).
8. Revise the (b) (4) to start with a positive statement such as “Bring to room temperature. Do not force thaw”. Additionally, we recommend using sentence case for improved readability.

B. Carton labeling

1. See A.1 through A.8 above
2. Relocate “Rx only” statement from the side panel to the principal display above the quantity statement.
3. Revise the quantity statement from “ (b) (4) to read “Contains 6 units of Single- Use bags. (b) (4)
 (b) (4) 12 units per case).

Best regards

Fariba Izadi, Pharm.D.
 Regulatory Health Project Manager
 Division of Anti-Infective Products
 Phone: (301) 796-0563
 Fax: (301) 796-9881
 E-mail: Fariba.Izadi@fda.hhs.gov

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/s/

FARIBA IZADI
05/08/2015



NDA 207131

INFORMATION REQUEST

Celerity Pharmaceuticals, LLC
Attention: Brent Yurschak, Senior Regulatory Affairs Manager
9450 W. Bryn Mawr Ave.
Suite 640
Rosemont, IL 60018

Dear Mr. Yurschak:

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

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a written response by February 20, 2015 in order to continue our evaluation of your NDA.

1. Section 3.2.S.4.2 indicates that the drug substance solution (b) (4) and we are trying to evaluate how this affects the (b) (4) of the drug product. We were not able to locate this information in the NDA. Please indicate where in the NDA it is presented or submit this information.
2. Provide details of the forced degradation study on the drug product with relevant chromatograms.

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 - 3815.

Sincerely,

{See appended electronic signature page}

Dorota Matecka, Ph.D.
Acting Branch Chief, Branch III
Division of New Drug Product I
Office of New Drug Products
Center for Drug Evaluation and Research

Dorota M.
Matecka -S

 Digitally signed by Dorota M. Matecka, S
DN: cn=US, o=U.S. Government, ou=FDA, ou=People
© 2015 19200900 100 1 1=150013291, cn=Dorota M. Matecka, S
Date: 2015.02.08 15:13:39 -0500

From: Bhandari, Navi
To: ["byurschak@celeritypharma.com"](mailto:byurschak@celeritypharma.com)
Bcc: [Zhang, Chunchun](#)
Subject: NDA 207131 Information Request
Date: Monday, April 06, 2015 9:49:00 AM
Importance: High

Dear Mr. Yurschak:

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

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a written response by April 20, 2015 in order to continue our evaluation of your NDA.

1. The "in-process controls" listed in Section 3.2.P.3.4-1 have the potential to impact critical quality attributes. Please identify the critical process parameters for the proposed manufacturing process based on preselection of operating ranges or magnitude of product quality response. Please note that changes from the preselected targets/ranges (i.e. changes outside of the Proven Acceptable Ranges) could have a minor, moderate or substantial potential to adversely affect product quality. The Agency's expectation is that the potential impact of changes to process parameters and in-process controls, including those designated as non-critical process parameters, as well as the parameters in Master Batch Record, be assessed under the firm's quality system at the time of the change. As appropriate, changes with a potential to adversely affect product quality should be notified to the Agency in accordance with 21 CFR 314.70. Based on the information submitted, we recommend designating the identified [REDACTED] (b) (4) [REDACTED] [REDACTED]
2. With reference to Table 1 in section 3.2.P.8.2 which provides details on the post-approval stability commitment we do not agree with [REDACTED] (b) (4) [REDACTED]. We recommend that you follow ICH Q1A(R2) in that the frequency of testing at long term storage condition should normally be every 3 months over the first year. Please submit the revised table updating the testing frequency.

Please provide confirmation of receipt for this message.

Thank you,

LT Navi Bhandari, Pharm.D, USPHS
Regulatory Business Process Manager
Office of Program and Regulatory Operations
Office of Pharmaceutical Quality
CDER/FDA
240-402-3815



NDA 207131

**FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED**

Celerity Pharmaceuticals, LLC
Attention: Brent Yurschak
Senior Regulatory Affairs Manager
9450 W. Bryn Mawr Avenue, Suite 640
Rosemont, IL 60018

Dear Mr. Yurschak:

Please refer to your New Drug Application (NDA) dated October 16, 2014, received October 16, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Cefazolin Injection, USP in GALAXY Container (2 g/100 mL).

We also refer to your amendment dated November 14, 2014.

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

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by June 23, 2015.

PRESCRIBING INFORMATION

Your proposed prescribing information (PI) must conform to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). We encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

During our preliminary review of your submitted labeling, we have identified the following labeling issues and have the following labeling comments or question:

Your proposed prescribing information (PI) does not conform to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#).

We request that you resubmit labeling (in Microsoft Word 2010 format) that addresses these issues concerning content and format by **January 18, 2015**. The resubmitted labeling will be used for further labeling discussions. Use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

Please respond only to the above requests for 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.

PROMOTIONAL MATERIAL

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

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

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

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

If you have any questions, call Fariba Izadi, PharmD, Regulatory Project Manager, at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

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

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/s/

KATHERINE A LAESSIG
12/16/2014



NDA 207131

NDA ACKNOWLEDGMENT

Celerity Pharmaceuticals, LLC
Attention: Brent Yurschak
Senior Regulatory Affairs Manager
9450 W. Bryn Mawr Avenue, Suite 640
Rosemont, IL 60018

Dear Mr. Yurschak:

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

Name of Drug Product: Cefazolin Injection, USP in GALAXY Container (2 g/100 mL)

Date of Application: October 16, 2014

Date of Receipt: October 16, 2014

Our Reference Number: NDA 207131

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 December 15, 2014, in accordance with 21 CFR 314.101(a).

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

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

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

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

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

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

If you have any questions, call Fariba Izadi, Pharm.D, Regulatory Health Project Manager, at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Frances V. LeSane
Chief, Project Management Staff
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

FRANCES V LESANE
10/30/2014



NDA 207131

MEETING MINUTES

Celerity Pharmaceuticals, LLC
Attention: Brent Yurschak
Senior Regulatory Affairs Manager
9450 W. Bryn Mawr Avenue, Suite 640
Rosemont, IL 60018

Dear Mr. Yurschak:

Please refer to your Pre-NDA meeting request submitted on March 24, 2014, for Cefazolin Injection, USP.

We also refer to the teleconference between representatives of your firm and the FDA on May 30, 2014. The purpose of the meeting was to discuss your plans to seek a waiver of the bioequivalence requirements for the premixed 2 g/100 mL Cefazolin Injection, USP drug product for the submission of an NDA via the 505(b)(2) pathway.

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

If you have any questions, call Fariba Izadi, PharmD, Regulatory Project Manager, at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes



**FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

MEMORANDUM OF MEETING MINUTES

Meeting Type: Meeting Type B
Meeting Category: Pre-NDA

Meeting Date and Time: May 30, 2014; 10:30 AM – 11:30 AM EST
Meeting Location: Teleconference

Application Number: NDA 207131
Product Name: Cefazolin Injection, USP
Indication: (b) (4)
Sponsor/Applicant Name: Celerity Pharmaceuticals

Meeting Chair: Sumathi Nambiar, MD, MPH
Meeting Recorder: Jane Dean, RN, MSN

FDA ATTENDEES

Elsbeth Chikhale, PhD	Biopharmaceutics Reviewer
Jane A. Dean, RN, MSN	Regulatory Health Project Manager
Kerian Grande, PhD	Clinical Microbiology Reviewer
Christopher Kadoorie, PhD	Statistics Reviewer
Peter Kim, MD	Clinical Reviewer
Dorota Matecka, PhD	Product Quality Team Lead
Sumathi Nambiar, MD, MPH	Director
David Roeder	Associate Director of Regulatory Affairs, Office of Antimicrobial Products
Daniel Rubin, PhD	Statistics Reviewer
Wendelyn Schmidt, PhD	Pharmacology/Toxicology Team Leader
Thomas Smith, MD	Clinical Team Leader
Kerry Snow, MS	Clinical Microbiology Team Leader

CELERITY ATTENDEES

Daniel Robins, PhD	President, Celerity
Ambareen Sheriff	Vice President, Regulatory Affairs and Quality Assurance, Celerity
Brent Yurschak	Senior Regulatory Affairs Manager, Celerity
George Monen	Senior Product Development Manager, Celerity
Gordon Johnston, RPh	Regulatory Consultant, Celerity
Glenn Dennis	Manager, Global Regulatory Affairs, Baxter

BACKGROUND

On March 24, 2014, Celerity Pharmaceuticals submitted a Pre-NDA type B meeting request. The briefing package was submitted on April 29, 2014 and contained Celerity's preliminary questions noted below. The Division provided preliminary comments to the questions via email on May 23, 2014. These are identified as **FDA Response**. On May 29, 2014, Celerity Pharmaceuticals submitted their request for additional clarifications. These are identified as **Celerity Clarification Request** in bold type. Discussion taking place at the meeting is captured under Meeting Discussion.

DISCUSSION

Chemistry, Manufacturing and Controls

Question 1

It is Celerity's position that during the manufacturing process, [REDACTED] (b) (4) [REDACTED] Does the Agency concur that the active ingredient in the final drug product is Cefazolin Sodium?

FDA Response:

Your proposal appears reasonable. However, you will need to provide a detailed description and characterization of your proposed drug product to include qualitative and quantitative composition and a description of the manufacturing process to demonstrate that cefazolin is present as a sodium salt in the proposed drug product. That should include a comparison of physico-chemical characteristics (e.g., concentration, sodium content, pH, osmolality, etc.) between your product and the reconstituted solution of the proposed listed drug.

Celerity Clarification Request: Are there any other physico-chemical characteristics in addition to concentration, sodium content, pH, and osmolality that the Agency feels would be appropriate to include in the application?

Meeting Discussion: The Division stated that the Applicant should provide test data to support the position that cefazolin is present as a sodium salt in the proposed drug product. The Division noted that physico-chemical characterization should include appearance and clarity of the solution to demonstrate that no visible particles are present in the drug product solution. In addition, the proposed specifications for the drug product should also include particulate matter requirements under USP <788>.

The Division asked Celerity to provide a comparison table (including qualitative and quantitative formula) between the Baxter 1 g drug product and the proposed Celerity 2 g drug product to fully characterize the product.

Clinical Pharmacology

Question 2

In accordance with 21 CFR § 320.22(a), Celerity intends to request a waiver of the requirement to submit in vivo bioavailability/bioequivalence data for the proposed 2 g/100 mL Cefazolin Injection, USP drug product. This request is based on 21 CFR § 320.22(b), which states that for certain drug products, the in vivo bioavailability or bioequivalence of the drug product may be self-evident provided:

- (1) The drug product:
 - (i) Is a parenteral solution intended solely for administration by injection, or an ophthalmic or otic solution; and
 - (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application.

The proposed drug product's self-evident in vivo bioavailability/bioequivalence is based on the fact that the product is an iso-osmotic, sterile solution intended solely for intravenous administration that has the same active ingredient in the same strength as the reference listed drug that is the subject of an approved NDA. Further, the dosage form, route of administration and dosing regimen for the proposed drug are the same as the RLD. The difference in product concentration (2 g/100 mL vs. 2 g/50 mL in RLD) and excipients (dextrose concentration of 4% vs. 3% in RLD and presence of sodium bicarbonate in the proposed product) are not expected to lead to clinical differences. Does the Agency concur with this position?

FDA Response:

Provided that there is agreement on the active ingredient discussed in question 1, your approach appears reasonable. In your NDA, submit a Biowaiver request along with a justification and all supportive information, such as a side-by-side comparison table between your proposed product and the listed drug, including components and composition, indication, stability, instructions for dilution, etc. Also provide pH and osmolality comparisons between the proposed drug product and the diluted listed drug. Justify any difference (e.g. delivered volume, infusion rate, amount of dextrose, etc.) between the listed drug and the proposed drug with respect to clinical safety and efficacy. The approvability of the Biowaiver request is a review issue under the NDA.

Celerity Clarification Request: For the osmolality comparison between the Celerity and RLD products, we propose to provide RLD data after initial dissolution and one day of storage at 25 °C. Does the Agency agree this is an acceptable approach?

Meeting Discussion: The Division confirmed that this approach was acceptable and asked Celerity to submit the data to the application.

Question 3

If the Agency concurs with the position presented in Question 2, does the Agency agree that from the clinical pharmacology perspective the provided information supports the sponsor's request for a waiver of the CFR requirement to submit in vivo bioavailability/bioequivalence data for their product, and that a biowaiver will be granted upon the forthcoming submission of the 505(b)(2) NDA?

FDA Response:

See response to question 2.

Meeting Discussion: No further discussion was necessary.

Drug Shortage

Question 4

Celerity has periodically monitored the drug shortage webpages of both the American Society of Health-System Pharmacists' (ASHP) and the FDA since December 19, 2013. Cefazolin Injection, USP has been listed on the ASHP webpage since at least December 19, 2013 and on the FDA webpage since March 31, 2014.

As of April 23, 2014, Cefazolin Injection, USP remains on both the ASHP and FDA drug shortage webpages.

Consistent with FDA's *Strategic Plan for Preventing and Mitigating Drug Shortages* document issued October 2013, does the Agency concur that an expedited review is appropriate for this NDA upon its submission in the third quarter of calendar year 2014 if the current shortage persists and Cefazolin Injection remains on the Agency's drug shortage list?

FDA Response

The review classification of the application will be determined once the NDA is filed.

Meeting Discussion: No further discussion was necessary.

Non-Clinical

Additional Comments:

You should demonstrate that the impurity/degradation profile of cefazolin injection in the Galaxy container stored as directed in your proposed label does not differ significantly from that of other marketed cefazolin products OR show that any impurities or degradation products in your product do not exceed the thresholds for qualification discussed in the applicable ICH guidance documents. If there are no impurities or degradation products that exceed the levels in a marketed product or ICH qualification threshold levels, no nonclinical testing of cefazolin injection in the Galaxy container will be needed. If there are impurities or degradation products that must be qualified, limited nonclinical testing would be needed.

Celerity Clarification Request: Celerity intends to provide impurity/degradation profile data for Baxter's currently marketed Cefazolin Injection, USP drug product under ANDA 063002 and compare it with data obtained from the proposed Celerity drug product. Does the Agency concur that if impurities or degradation products in the Celerity drug product do not differ significantly from the levels in the Baxter marketed drug product, no nonclinical testing of the Celerity drug product will be needed?

Meeting Discussion: The Division confirmed that this approach was acceptable.

PREA REQUIREMENTS

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

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (PSP) within 60 days of an End of Phase (EOP2) meeting. The PSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The PSP should be submitted in PDF and Word format.

For additional guidance on the timing, content, and submission of the PSP, including a PSP Template, please refer to the draft guidance for industry, *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans* at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.pdf>. In addition, you may contact the Pediatric and Maternal Health Staff at 301-796-2200 or email pdit@fda.hhs.gov. For further guidance on pediatric product development, please refer to: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm049867.htm>.

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). As you develop your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

505(b)(2) REGULATORY PATHWAY

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

If you intend to submit a 505(b)(2) application that relies for approval, in part, on FDA's finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a "bridge" (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified.

If you intend to rely, in part, on literature or other studies for which you have no right of reference but that are necessary for approval, you also must establish that reliance on the studies described in the literature or on the other studies is scientifically appropriate. You should include a copy of such published literature in the 505(b)(2) application and identify any listed drug(s) described in the published literature (e.g. trade name(s)).

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

If you propose to rely on FDA's finding of safety and/or effectiveness for a listed drug that has been discontinued from marketing, the acceptability of this approach will be contingent on FDA's consideration of whether the drug was discontinued for reasons of safety or effectiveness.

We encourage you to identify each section of your proposed 505(b)(2) application that relies on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature. In your 505(b)(2) application, we encourage you to clearly identify (for each section of the application, including the labeling): (1) the information for the proposed drug product that is

provided by reliance on FDA’s finding of safety and/or effectiveness for the listed drug or by reliance on published literature; (2) the “bridge” that supports the scientific appropriateness of such reliance; and (3) the specific name (e.g., proprietary name) of each listed drug named in any published literature on which your marketing application relies for approval. If you are proposing to rely on published literature, include copies of the article(s) in your submission.

In addition to identifying in your annotated labeling the source(s) of information essential to the approval of your proposed drug that is provided by reliance on FDA’s previous finding of safety and efficacy for a listed drug or by reliance on published literature, we encourage you to also include that information in the cover letter for your marketing application in a table similar to the one below.

List the information essential to the approval of the proposed drug that is provided by reliance on the FDA’s previous finding of safety and efficacy for a listed drug or by reliance on published literature	
Source of information (e.g., published literature, name of listed drug)	Information Provided (e.g., specific sections of the 505(b)(2) application or labeling)
<i>1. Example: Published literature</i>	<i>Nonclinical toxicology</i>
<i>2. Example: NDA XXXXXX “TRADENAME”</i>	<i>Previous finding of effectiveness for indication X</i>
<i>3. Example: NDA YYYYYY “TRADENAME”</i>	<i>Previous finding of safety for Carcinogenicity, labeling section XXX</i>
<i>4.</i>	

Please be advised that circumstances could change that would render a 505(b)(2) application for this product no longer appropriate. For example, if a pharmaceutically equivalent product were approved before your application is submitted, such that your proposed product would be a “duplicate” of a listed drug and eligible for approval under section 505(j) of the FD&C Act, then it is FDA’s policy to refuse to file your application as a 505(b)(2) application (21 CFR 314.101(d)(9)). In such a case, the appropriate submission would be an Abbreviated New Drug Application (ANDA) that cites the duplicate product as the reference listed drug.

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/s/

SUMATHI NAMBIAR
06/25/2014