

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**50-809**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

New Drug Application – 505(b)(2)  
Azithromycin for Injection, 500 mg/vial and 2.5 g/vial  
Module 1: Administrative Information and Prescribing Information

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1.3.2.1 *No Relevant Patents Statement*

As required by 21 CFR § 314.54(a)(1)(vi) and 21 CFR § 314.94(a)(12)(ii), SICOR Pharmaceuticals, Inc., hereby certifies that, in its opinion and to its best knowledge, there are **no** patents that claim the listed drug referred to in this application, or that claim a use of the listed drug referred to in this application, or that claim the use of the listed drug.

Provided in **Attachment 3** is the requisite Form FDA 3542a *Patent Information Submitted with the Filing of an NDA, Amendment, or Supplement*.

Rosalie A. Lowe  
Rosalie A. Lowe  
Director, Regulatory Affairs

29 July 2005  
Date

## EXCLUSIVITY SUMMARY

NDA # 50-809

SUPPL #

HFD # 520

Trade Name

Generic Name azithromycin citrate

Applicant Name Scior Pharmaceuticals

Approval Date, If Known 12/21/06

### PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES  NO

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

505(b)(2)

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

YES  NO

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

The Sponsor is relying on data (safety and efficacy) from Pfizer's Zithromax Injection. The Scior product is a citrate salt that once reconstituted is the same azithromycin as Pfizer's.

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

d) Did the applicant request exclusivity?

YES  NO

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

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

YES  NO

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

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

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

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

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

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

Investigation #1  
IND #                      YES                       ! NO   
! Explain:

Investigation #2  
IND #                      YES                       ! NO   
! Explain:

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

Investigation #1

YES

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:

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Name of person completing form: Carmen DeBellas

Title: Regulatory Project Manager

Date: 12/11/06

Name of Office/Division Director signing form: Janice M. Soreth, MD

Title: Division Director

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

**New Drug Application – 505(b)(2)**  
**Azithromycin for Injection, 500 mg/vial and 2.5 g/vial**  
**Module 1: Administrative Information and Prescribing Information**

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1.3.4 Debarment Certification

As required by the Generic Drug Enforcement Act of 1992, SICOR Pharmaceuticals, Inc., certifies that we have not nor will we use in any capacity the services of any person debarred under subsections (a) or (b) [section 306 (a) or (b)] of the Act, in connection with our application for Azithromycin for Injection.

There have been no convictions of crimes (as specified in section 306 (a) and (b) of the Act) within the previous five years of any SICOR Pharmaceuticals employees or affiliated company, or employees of the affiliated companies responsible for the development or submission of this abbreviated application for Azithromycin for Injection.

Rosalie A. Lowe  
Rosalie A. Lowe  
Director, Regulatory Affairs

29 July 2005  
Date



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 50-809

INFORMATION REQUEST LETTER

Sicor Pharmaceuticals, Inc.  
Attention: Sonia Hernandez  
Manager, Regulatory Affairs  
19 Hughes  
Irvine, CA 92618

Dear Ms. Hernandez:

Please refer to your August 2, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Azithromycin for Injection.

We also refer to your submission dated June 16, 2006.

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

If you have any questions, call Linda Mullins Athey, Regulatory Health Project Manager for Quality, at 301-796-2096.

Sincerely,

*{See appended electronic signature page}*

Norman Schmuff, Ph.D.  
Branch Chief  
Division of Pre-Marketing Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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

-----  
Norman Schmuff  
12/12/2006 08:53:00 AM



SICOR Pharmaceuticals, Inc.  
A subsidiary of TEVA Pharmaceuticals USA  
19 Hughes  
Irvine, CA 92618-1902  
Phone: 800.806.4226  
Fax: 949.855.8210

December 8, 2006

James D. Vidra, Ph.D.  
Chemistry Team Leader for the Division of  
Anti-Infective and Ophthalmology Products  
DNDC Office of New Drug Chemistry  
Center for Drug Evaluation and Research  
Central Documentation Room, 5901-B  
Ammendale Road  
Beltsville, MD 20705-1266

RE: Azithromycin for Injection  
500 mg/vial and 2.5 g/vial  
505(b)(2) NDA 50-809

#### AMENDMENT- CHEMISTRY

Dear Dr. Vidra:

Reference is made to SICOR's NDA 50-809, for Azithromycin for Injection, 500 mg/vial and 2.5 g/vial, which was submitted to the Agency on January 31, 2006. Further reference is made to a telephone conversation between Mr. Carmen DeBellas, FDA and Sonia Hernandez on December 8, 2006.

In accordance with the provisions of Section 314.60 of the *Code of Federal Regulations, Title 21*, we hereby amend our application to provide the requested information.

1. SICOR commits to modifying and validating the analytical method, QCP-1494, "Assay and Purity Determinations for Azithromycin in the Drug Substance and Drug Products by HPLC". Specifically, SICOR will establish the appropriate and separate concentrations for the assay test preparations and related compound test preparations. The analytical method will be validated accordingly. The revised method and validation report will be submitted to the Agency by April 15, 2007.
2. SICOR commits to manufacturing the drug product with \_\_\_\_\_
3. SICOR commits to provide the Pediatric Assessment Final Study Report by Q4 2009.

James D. Vidra, Ph. D.

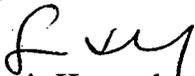
December 8, 2006

Page Two

Additionally, we are providing 24 month stability test results on all exhibit stability lots.

We trust you will find the information in this amendment satisfactory for your review and approval. If there are any questions concerning this application, please do not hesitate in contacting me at (949) 455-4779. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,



Sonia Hernandez

Associate Director, Regulator Affairs

S:\Azithromycin 50-809\AMEND\Amend 9-15-06.doc

cc: Mr. Alonza Cruse, Director  
FDA, Los Angeles District

1 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

       § 552(b)(4) Draft Labeling

       § 552(b)(5) Deliberative Process

## ACTION PACKAGE CHECKLIST

Application Information		
A # JA # 50-809	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type NDA
Proprietary Name: azithromycin citrate Established Name: Dosage Form: injection.		Applicant: Scior Pharmaceuticals, Inc.
RPM: DeBellas		Division: 520      Phone # 6-1203
<p>NDA Application Type:    <input type="checkbox"/> 505(b)(1)    <input checked="" type="checkbox"/> 505(b)(2)</p> <p>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 NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>	<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>NDA 50-733 Zithromax (azithromycin) Injection</p> <p>Provide a brief explanation of how this product is different from the listed drug. It is a lyophilized powder of azithromycin citrate</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p><b>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</b></p> <p><input checked="" type="checkbox"/> Confirmed      <input type="checkbox"/> Corrected Date: 12/11/07</p>	
<p>❖ User Fee Goal Date</p> <p>❖ Action Goal Date (if different)</p>		12/21/06
❖ Actions		
<ul style="list-style-type: none"> <li>• Proposed action</li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>• Previous actions (<i>specify type and date for each action taken</i>)</li> </ul>		<input type="checkbox"/> None AE 6/02/06
<p>❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)</p>		<input checked="" type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):  NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2  <input type="checkbox"/> Orphan drug designation  NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies  NDAs and NDA Supplements: <input type="checkbox"/> OTC drug  Other:  Other comments:	
❖ Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> <li>Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>This application is on the AIP                             <ul style="list-style-type: none"> <li>Exception for review (<i>file Center Director's memo in Administrative Documents section</i>)</li> <li>OC clearance for approval (<i>file communication in Administrative Documents section</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> <li>Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Press Office notified of action</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<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

❖ <b>Exclusivity</b>	
<ul style="list-style-type: none"> <li>• NDAs: Exclusivity Summary (approvals only) (<i>file Summary in Administrative Documents section</i>)</li> </ul>	<input type="checkbox"/> Included
<ul style="list-style-type: none"> <li>• Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>• NDAs/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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>• NDAs: 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>)</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>• NDAs: 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>)</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>• NDAs: 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>)</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
❖ <b>Patent Information (NDAs and NDA supplements only)</b>	
<ul style="list-style-type: none"> <li>• 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.</li> </ul>	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> <li>• 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.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified  21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>• [505(b)(2) applications] If the application includes a <b>paragraph III</b> 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).</li> </ul>	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> <li>• [505(b)(2) applications] For each <b>paragraph IV</b> 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>)</li> </ul>	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified
<ul style="list-style-type: none"> <li>• [505(b)(2) applications] For each <b>paragraph IV</b> certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.</li> </ul> <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner's receipt of the applicant's</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No

notice of certification?

(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 to the next section below (Summary Reviews).

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

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

Yes  No

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

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

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

Yes  No

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

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

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

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 written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced

<p>within the 45-day period).</p> <p>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).</p> <p>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</p>	
<b>Summary Reviews</b>	
❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)	
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)	
<b>Labeling</b>	
❖ Package Insert	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	6/07/06
• Original applicant-proposed labeling	7/26/05
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Patient Package Insert	
• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	
❖ Medication Guide	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	
• Original applicant-proposed labeling	
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (full color carton and immediate-container labels)	
• Most-recent division-proposed labels (only if generated after latest applicant submission)	
• Most recent applicant-proposed labeling	6/02/06
❖ Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)	<input checked="" type="checkbox"/> DMETS <input type="checkbox"/> DSRCS <input checked="" type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input type="checkbox"/> Other reviews <input type="checkbox"/> Memos of Mtgs

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting, ADRA) (indicate date of each review)	
NDA and NDA supplement approvals only: Exclusivity Summary (signed by Division Director)	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> <li>Center Director's Exception for Review memo</li> <li>If AP: OC clearance for approval</li> </ul>	
❖ Pediatric Page (all actions)	<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. (Include certification.)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies	<input type="checkbox"/> None
<ul style="list-style-type: none"> <li>Outgoing Agency request for post-marketing commitments (if located elsewhere in package, state where located)</li> <li>Incoming submission documenting commitment</li> </ul>	12/08/06
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	included
❖ Internal memoranda, telecons, email, etc.	
❖ Minutes of Meetings	
<ul style="list-style-type: none"> <li>Pre-Approval Safety Conference (indicate date; approvals only)</li> <li>Pre-NDA/BLA meeting (indicate date)</li> <li>EOP2 meeting (indicate date)</li> <li>Other (e.g., EOP2a, CMC pilot programs)</li> </ul>	N/A
	<input checked="" type="checkbox"/> No mtg
	<input checked="" type="checkbox"/> No mtg
❖ Advisory Committee Meeting	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> <li>Date of Meeting</li> <li>48-hour alert or minutes, if available</li> </ul>	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
CMC/Product Quality Information	
❖ CMC/Product review(s) (indicate date for each review)	5/26/06
Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications)	
<ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</li> <li><input type="checkbox"/> Review &amp; FONSI (indicate date of review)</li> <li><input type="checkbox"/> Review &amp; Environmental Impact Statement (indicate date of each review)</li> </ul>	
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (indicate date of each review)	5/30/06 <input type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection	
<ul style="list-style-type: none"> <li>NDAs: Facilities inspections (include EER printout)</li> </ul>	Date completed: See Review <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> <li>• Facility review (<i>indicate date(s)</i>)</li> <li>• Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>)</li> </ul>	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
<b>Nonclinical Information</b>	
❖ Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )	N/A
❖ 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	N/A
❖ Nonclinical inspection review Summary (DSI)	<input checked="" type="checkbox"/> None requested
<b>Clinical Information</b>	
❖ Clinical review(s) ( <i>indicate date for each review</i> )	6/02/06
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	N/A
❖ Clinical consult reviews from other review disciplines/divisions/Centers ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> None
❖ Microbiology (efficacy) reviews(s) ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> Not needed
❖ Safety Update review(s) ( <i>indicate location/date if incorporated into another review</i> )	N/A
❖ Risk Management Plan review(s) (including those by OSE) ( <i>indicate location/date if incorporated into another review</i> )	N/A
❖ Controlled Substance Staff review(s) and recommendation for scheduling ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) ( <i>include copies of DSI letters to investigators</i> )	<input checked="" type="checkbox"/> None requested
<ul style="list-style-type: none"> <li>• Clinical Studies</li> <li>• Bioequivalence Studies</li> <li>• Clin Pharm Studies</li> </ul>	
❖ Statistical Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None      5/26/06

Comment [11]:

## Appendix A 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 Office of Regulatory Policy representative.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 50-809

Sicor Pharmaceuticals, Inc.  
Attention: Sonia Hernandez  
Manager, Regulatory Affairs  
19 Hughes  
Irvine, CA 92618

Dear Ms. Hernandez:

Please refer to your New Drug Application (NDA) dated July 29, 2006, received August 2, 2006 submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Azithromycin Citrate for Injection 500 mg/vial and 2.5 g/vial

We have reviewed the referenced material and have the following comments and recommendations.

1. 
  - 2.
  3. Identify which  (original or alternate) was used when stability data were presented in the updated amendment. 
  4. In the Container Closure section of Azithromycin for Injection, list all container components that are in contact with the drug solution. In addition, perform the extractable and leachable studies with the component that are in contact with the drug solution.
  5. List or reference any relevant USP test that was performed for the package components mentioned in the discussion above.
  6. The NDA contains limited stability data (12 months). The DMF also contains limited stability for azithromycin hydrogencitrate. The limited stability data has made shelf life projection difficult. Please update the NDA with more stability data as soon as possible.
  7. The DMF was reviewed and specific deficiencies were sent to the DMF holder.
  8. In reference to Section 3.2.S.4 (p2121/vol 2) of Azithromycin for Injection, explain why there are wide variations in the recovery of various drug impurities ranging from 
  9. Provide more details about the recovery study mentioned in #5.
  10. Provide either a full environmental assessment of Azithromycin Citrate for Injection, or alternatively project the consumption for 5 years and compute EIC to determine eligibility for exclusion. If the criteria of EIC <1ppm is met and no extraordinary conditions exist an Environmental Assessment exclusion may be claimed, Environmental Assessment evaluation based on information from the proprietary manufacturer alone is not complete.
  11. Clarify (on page 1025) what is a "". Provide secondary package labels and samples if vials are further packaged.
  12. Provide a brief summary describing the critical process control for lyophilization/manufacturing of the drug product.
  13. 
- 

14. Regarding the specification of azithromycin injection submitted in Table 2.3. P.5-1 & 2, page 1089 and Table 2.3.S.4.2, page 1078, it is recommended that the relevant USP tests be applied to drug substance and drug product specifications and included in the submission. You may simply list the USP test # in the specification table. In some tables, USP tests were listed and others not, simply confirm or clarify. Several examples are listed below; refer to the current USP for full details for injection dosage forms. If different tests are proposed, confirm the tests you proposed are equivalent or better.

Crystallinity	USP <695>
pH	USP <791>
Water, % w/w	USP <921>
Bacterial endotoxins	USP<85>
Sterility	USP <71>
Particulate Matter	USP<788>
Residue on ignition	USP<281>
Heavy metal	USP<231>
Specific rotation	USP<781>

15. The assay acceptance criteria should be as a percent of the label claim for azithromycin hydrogencitrate, which brackets 100%. The acceptance criteria should be equal or better than the comparable base in the USP.
16. No "Attachment 1" containing "the Letter of Authorization LOA for the \_\_\_\_\_ was found as indicated in the amendment dated 1/31/06. An (LOA) for the \_\_\_\_\_ was

17.

18.

19.

20.

21.

Labeling General Comments:

1.

2. 

3.

5

6. 

Container Labeling (Single Dose Vial: 500 mg/mL):

1. 

2.

3. 

1

Container Labeling (Pharmacy Bulk Vial: 2.5 gram/vial):

1. 

Tray Labeling:

1. 

2.

Carton Labeling:

1. 

Insert Labeling:

1. 

2. 

3.

4.

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

Sincerely,

*{See appended electronic signature page}*

Janice M. Soreth, MD  
Division Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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

-----  
Janice Soreth

6/2/2006 03:08:55 PM

**NDA REGULATORY FILING REVIEW**  
**(Including Memo of Filing Meeting)**

NDA # 50-809

Supplement #

Efficacy Supplement Type SE-

Trade Name:

Established Name: azithromycin injection

Strengths: 500 mg vial and 2.5 g/vial

Applicant: Scior Pharmaceuticals

Agent for Applicant:

Date of Application: July 29, 2005

Date of Receipt: August 2, 2005

Date clock started after UN:

Date of Filing Meeting: September 28, 2005

Filing Date: October 1, 2005

Action Goal Date (optional):

User Fee Goal Date: June 2, 2006

Indication(s) requested: Community Acquired Pneumonia  
Pelvic Inflammatory Disease

Type of Original NDA:

(b)(1)

(b)(2)

OR

Type of Supplement:

(b)(1)

(b)(2)

**NOTE:**

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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). If the application is a (b)(2), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

NDA is a (b)(1) application

OR

NDA is a (b)(2) application

Therapeutic Classification: S

P

Resubmission after withdrawal?

Resubmission after refuse to file?

Chemical Classification: (1,2,3 etc.) 3

Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted:

YES  NO

User Fee Status:

Paid

Exempt (orphan, government)

Waived (e.g., small business, public health)

**NOTE:** If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the

Version: 12/15/2004

This is a locked document. If you need to add a comment where there is no field to do so, unlock the document using the following procedure. Click the 'View' tab; drag the cursor down to 'Toolbars'; click on 'Forms.' On the forms toolbar, click the lock/unlock icon (looks like a padlock). This will allow you to insert text outside the provided fields. The form must then be relocked to permit tabbing through the fields.

*product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.*

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES  NO   
If yes, explain:
- Does another drug have orphan drug exclusivity for the same indication? YES  NO
- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES  NO   
If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).
- Is the application affected by the Application Integrity Policy (AIP)? YES  NO   
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES  NO
- Does the submission contain an accurate comprehensive index? YES  NO
- Was form 356h included with an authorized signature? YES  NO   
**If foreign applicant, both the applicant and the U.S. agent must sign.**
- Submission complete as required under 21 CFR 314.50? YES  NO   
If no, explain:
- If an electronic NDA, does it follow the Guidance? N/A  YES  NO   
**If an electronic NDA, all forms and certifications must be in paper and require a signature.**  
Which parts of the application were submitted in electronic format?  
Additional comments:
- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A  YES  NO
- Is it an electronic CTD (eCTD)? N/A  YES  NO   
**If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.**  
Additional comments:
- Patent information submitted on form FDA 3542a? YES  NO
- Exclusivity requested? YES, \_\_\_\_\_ Years NO   
*NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*
- Correctly worded Debarment Certification included with authorized signature? YES  NO   
**If foreign applicant, both the applicant and the U.S. Agent must sign the certification.**

**NOTE:** Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e.,  
 “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as “To the best of my knowledge . . . .”

- Financial Disclosure forms included with authorized signature? YES  NO   
**(Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)**  
**NOTE:** Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section)? Y  NO
- PDUFA and Action Goal dates correct in COMIS? YES  NO   
 If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: None
- End-of-Phase 2 Meeting(s)? Date(s) None NO   
 If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) None NO   
 If yes, distribute minutes before filing meeting.

**Project Management**

- Was electronic “Content of Labeling” submitted? YES  NO   
 If no, request in 74-day letter.
- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES  NO
- Risk Management Plan consulted to ODS/IO? N/A  YES  NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y  NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A  YES  NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A  YES  NO

**If Rx-to-OTC Switch application:**

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A  YES  NO
- Has DOTCDP been notified of the OTC switch application? YES  NO

**Clinical**

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?  
YES  NO

**Chemistry**

- Did applicant request categorical exclusion for environmental assessment? YES  NO   
If no, did applicant submit a complete environmental assessment? YES  NO   
If EA submitted, consulted to Florian Zielinski (HFD-357)? YES  NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES  NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES  NO

ATTACHMENT

**MEMO OF FILING MEETING**

DATE: September 28, 2005

**BACKGROUND:** Sicor's azithromycin for injection is offered in a single –dose vial at 500mg/vial, is formulated using the same active moiety and inactive ingredients, and offered in the same dosage form, strength, and route of administration as Pfizer's Zithromax,

(Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES: Janice Soreth Division Director  
John Alexander Clinical Team Leader  
Charles Bonapace Clinical Pharmacology Reviewer  
Nasim Moledina Clinical Reviewer  
Andrew Yu Chemistry Reviewer  
David Roeder Associate Director of Regulatory Affairs  
Elaine Tseng Regulatory Counsel  
Venkateswar Jarugula Clinical Pharmacology Team Leader  
James Vidra Chemistry Team Leader  
Jeffrey Tworzyanski Clinical Pharmacology Reviewer  
Carmen DeBellas Project Manager

ASSIGNED REVIEWERS (including those not present at filing meeting) : -

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Nasim Moledina
Secondary Medical:	John Alexander
Statistical:	
Pharmacology:	
Statistical Pharmacology:	
Chemistry:	Andrew Yu
Environmental Assessment (if needed):	
Biopharmaceutical:	Jeffrey Tworzyanski
Microbiology, sterility:	Steven Langille
Microbiology, clinical (for antimicrobial products only):	
DSI:	
Regulatory Project Management:	Carmen DeBellas
Other Consults:	

Per reviewers, are all parts in English or English translation? YES  NO   
If no, explain:

CLINICAL FILE  REFUSE TO FILE

- Clinical site inspection needed? YES  NO
- Advisory Committee Meeting needed? YES, date if known \_\_\_\_\_ NO

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

	N/A	<input checked="" type="checkbox"/>	YES	<input type="checkbox"/>	NO	<input type="checkbox"/>
CLINICAL MICROBIOLOGY	N/A	<input checked="" type="checkbox"/>	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
STATISTICS	N/A	<input checked="" type="checkbox"/>	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
BIOPHARMACEUTICS			FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
					YES	<input type="checkbox"/>
					NO	<input checked="" type="checkbox"/>
PHARMACOLOGY	N/A	<input checked="" type="checkbox"/>	FILE	<input type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
					YES	<input type="checkbox"/>
					NO	<input checked="" type="checkbox"/>
CHEMISTRY			FILE	<input checked="" type="checkbox"/>	REFUSE TO FILE	<input type="checkbox"/>
					YES	<input checked="" type="checkbox"/>
					NO	<input type="checkbox"/>
					YES	<input checked="" type="checkbox"/>
					NO	<input type="checkbox"/>

**ELECTRONIC SUBMISSION:**

Any comments: None

**REGULATORY CONCLUSIONS/DEFICIENCIES:**

**(Refer to 21 CFR 314.101(d) for filing requirements.)**

- The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
  - No filing issues have been identified.
  - Filing issues to be communicated by Day 74. List (optional):

**ACTION ITEMS:**

1.  If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
2.  If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3.  Convey document filing issues/no filing issues to applicant by Day 74.

Carmen DeBellas, RPh  
Regulatory Project Manager, HFD-

**APPEARS THIS WAY  
ON ORIGINAL**

### Appendix A to NDA Regulatory Filing Review

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

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of **another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product)** to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) 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.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

**Appendix B to NDA Regulatory Filing Review  
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES  NO

*If "No," skip to question 3.*

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s): NDA 50-733 Zithromax
3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?

YES  NO

*(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))*

*If "No," skip to question 4. Otherwise, answer part (b).*

- (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES  NO   
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

*If "Yes," skip to question 6. Otherwise, answer part (c).*

- (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)?

YES  NO

*If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

4. (a) Is there a pharmaceutical alternative(s) already approved? YES  NO

*(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)*

*If "No," skip to question 5. Otherwise, answer part (b).*

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES  NO   
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

**NOTE:** *If there is more than one pharmaceutical alternative approved, consult the Director, Division of*

*Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.*

*If "Yes," skip to question 6. Otherwise, answer part (c).*

- (c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES  NO

*If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product? YES  NO

*If "No," skip to question 6.*

*If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.*

- (b) Is the approved drug product cited as the listed drug? YES  NO

6. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

The Sicor product is manufactured using a different form of Azithromycin – Azithromycin Hydrogenecitrate rather than Azithromycin Dihydrate

7. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)). YES  NO
8. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES  NO
9. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES  NO
10. Are there certifications for each of the patents listed for the listed drug(s)? YES  NO
11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)  
Patent number(s):

- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)  
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)  
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)  
Patent number(s):

**NOTE:** *IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must subsequently submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)].*

- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)  
Patent number(s):
- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).  
Patent number(s):
- Written statement from patent owner that it consents to an immediate effective date upon approval of the application.  
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?  
YES  NO

- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?  
YES  NO

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?  
N/A  YES  NO

- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv)).?  
N/A  YES  NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).  
YES  NO

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.  
YES  NO

- EITHER

The number of the applicant's IND under which the studies essential to approval were conducted.

IND# N/A NO

OR

A certification that the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

YES  NO

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES  NO

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/s/

-----  
Carmen DeBellas

5/23/2006 03:22:41 PM

CSO

**Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications**

**MEMORANDUM**

---

**\*\*Pre-Decisional Agency Information\*\***

**Date:** May 12, 2006  
**To:** Carmen Debellas, Project Manager  
Division of Anti-Infective and Ophthalmology Products  
**From:** Sheila Ryan, Pharm.D.  
Division of Drug Marketing, Advertising, and Communications  
**Subject:** NDA 50-809 Azithromycin for Injection

---

DDMAC has reviewed the proposed product labeling (PI) for Azithromycin for Injection and we offer the following comments. Please feel free to contact me with any questions or clarifications.

**DESCRIPTION**

1. Are the proposed Table 1 and Table 2 necessary?

[

]

We recommend deleting these tables and renumbering the remaining tables included in the label.

**MICROBIOLOGY**

2. From the proposed label:

***“Aerobic and facultative gram-positive microorganisms***

*Staphylococcus aureus*  
*Streptococcus pneumoniae*

*NOTE: Azithromycin demonstrates cross-resistance with erythromycin-resistant gram-positive strains. Most strains of Enterococcus faecalis and methicillin-resistant staphylococci are resistant to azithromycin for injection.”*

This section is inconsistent with the label for Zithromax. Is it necessary and appropriate to list these organisms twice (here under the section dealing with the injection uses and the section dealing with the oral tablets and suspension uses)? Did this sponsor specifically perform susceptibility tests for these organisms with the injection form? If not, we recommend deleting.

In addition, is the information contained in the "NOTE" clinically significant? We note this information is not included in the Zithromax label. If this information is to be included in the label, we recommend moving the NOTE to the "Aerobic and facultative gram-positive microorganisms" section under the oral tablets and suspension uses listed further down in the Microbiology section.

### **HOW SUPPLIED**

3. The "Directions for Proper Use of Azithromycin for Injection PHARMACY BULK PACKAGE" appears to be misplaced here. This information is more appropriate for the Dosage and Administration section of the label.
4. From the proposed label:

*"The container closure may be penetrated only time, utilizing a suitable transfer device."*

We recommend revising this statement to read:

The container closure maybe penetrated only one time, utilizing a suitable transfer device.

### **CONAINTER AND CARTON LABELS**

DDMAC has no comments on the carton and container labels at this time.

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/s/

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Sheila Ryan  
5/12/2006 01:23:52 PM  
DDMAC REVIEWER

# NDA 50-809

## Azithromycin For Injection from Sicor Pharmaceuticals

### List Of Deficiencies and Comments To Be faxed to Sicor (4/15/06)

1. No "Attachment 1" containing "the LOA for the " was found as indicated in the amendment dated 1/31/06.

2.

3.

4.

5.

6.

7. Please identify which  (original or alternate) were used when stability data were presented in the updated amendment.

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/s/

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Carmen DeBellas  
4/17/2006 03:29:07 PM  
CSO



FOOD AND DRUG ADMINISTRATION  
Center for Drug Evaluation and Research

Facsimile Transmittal Cover

Date: 3/20/06 Total number of pages (including cover): 2  
To: SONIA HERNANDEZ From: ROBERT HUMMEL  
Organization: SICOR Organization: Office of New Drug Quality Assessment  
Division of Pre-Marketing Assessment  
Address: Address: 10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Fax No.: 949-583-7351 Fax No.: 301-796-9850  
Telephone No.: Telephone No.: 301-796-1981  
Comment:

NDA 50-849

AZITHROMYCIN FOR INJECTION

CMC DEFICIENCIES / COMMENTS

PLEASE EMAIL ME YOUR RESPONSE  
TO [robert.hummel@fda.hhs.gov](mailto:robert.hummel@fda.hhs.gov), if you  
HAVE SECURE/ENCRYPTED E-MAIL. BOB

This document is intended only for the use of the party to whom it is addressed and may contain information that is privileged, confidential and protected from disclosure under applicable law. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

# NDA 50-809

## Azithromycin For Injection from Sicor Pharmaceuticals

### List Of Deficiencies and Comments To Be faxed to Sicor (3/16/06)

1. Regarding the specifications of azithromycin injection submitted under Table 2.3.p.5-1 & 2, page 1089 and Table 2.3.S.4.2, page 1078, the reviewer recommends that the relevant USP tests be applied to drug substance and drug product specifications and included in the submission. You may simply list the USP test# in the specification table. In some tables, USP tests were listed and others not, please simply confirm or clarify.

Several examples are listed below, please refer to the current USP for full details for injection dosage forms. If different tests are proposed, please confirm the tests you proposed are equivalent or better.

Crystallinity	USP <695>
pH	USP <791>
Water, % w/w	USP <921>
Bacterial endotoxins	USP <85>
Sterility	USP <71>
Particulate Matter	USP <788>
Residue on ignition	USP <281>
Heavy metal	USP <231>
Specific rotation	USP <781S>

2. The assay acceptance criteria should be as a percent of label claim for azithromycin hydrogencitrate, which brackets 100%. The acceptance criteria should be equal or better than the comparable base in USP.

3.



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/s/

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Robert Hummel  
3/26/2006 04:17:38 PM  
PROJECT MANAGER FOR QUALITY



FOOD AND DRUG ADMINISTRATION

Center for Drug Evaluation and Research

Facsimile Transmittal Cover

Date: 3/2/06 Total number of pages (including cover): 2

To: SONIA HERNANDEZ From: ROBERT HUMMEL

Organization: SICOR PHARMACEUTICALS Organization: Office of New Drug Quality Assessment  
Division of Pre-Marketing Assessment

Address: Address: 10903 New Hampshire Avenue  
Silver Spring, MD 20993-002

Fax No.: 949-583-7351 Fax No.: 301-796-9850

Telephone No.: 949-455-4779 Telephone No.: 301-796-1981  
Comment: \_

NDA 50-809

DEFICIENCIES + COMMENTS

PLEASE RESPOND AS SOON AS POSSIBLE

THANKS, BOB

This document is intended only for the use of the party to whom it is addressed and may contain information that is privileged, confidential and protected from disclosure under applicable law. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

# NDA 50-809

## Azithromycin for Injection from Sicor Pharmaceuticals

### List of Deficiencies and Comment to be faxed to Sicor

1. The NDA was filed with limited stability data (3-6 months). An amendment with 12-months of update has been received in Feb 2006. However, because there is limited stability for azithromycin hydrogencitrate in the DMF, shelf life projection is difficult. Will Sicor be updating the NDA with more stability data in the next two months?
2. Azithromycin bulk was supplied by \_\_\_\_\_ (DMF \_\_\_\_\_). The DMF on file was initially incomplete without the \_\_\_\_\_ An update has just been received to address this issue, other specific DMF deficiencies will be sent to the DMF holder directly.
3. Under the Container Closure section of Azithromycin for Injection, please list all container components that are in contact with the drug solution. Has extractable and leachable studies been performed with the components that are in contact with the drug solution?
4. Please list or reference any relevant USP test that was performed for the package components mentioned in #3 above.
5. In Section 3.2.S4 (p2121/Vol 2) of Azithromycin for Injection, please explain why there is wide variation in the recovery of various drug impurities ranging from \_\_\_\_\_
6. Please provide more details about the recovery study in #5 above.
7. Under the section on EA, Sicor should provide environmental evaluation of Azithromycin for injection and determine if its consumption based on 5 years of projection to determine EIC and eligibility for exclusion. If the criterion of EIC < 1ppm is met and there are no extraordinary conditions existing, EA exclusion may be claimed, otherwise, Sicor should submit its own EA evaluation (not based on the proprietary manufacturer).
8. On page 1025, please clarify what is a "\_\_\_\_\_". There is no reference to "\_\_\_\_\_" elsewhere. Please update secondary package labels if vials are further packaged. For clarity, please provide sample and labels if available.
9. In module 2, under 2.3, the quality overall summary was presented with a brief description of the drug product and a chemical name. There was a summary of the microbiological and sterility control. Please provide also a brief summary describing the critical process control for lyophilization/manufacturing of the drug product.

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/s/

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Robert Hummel  
3/2/2006 03:06:43 PM



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 50-809

**DISCIPLINE REVIEW LETTER**

Sicor Pharmaceuticals, Inc.  
Attention: Sonia Hernandez  
Manager, Regulatory Affairs  
19 Hughes  
Irvine, CA 92618

Dear Ms. Hernandez:

Please refer to your July 29, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for azithromycin for injection.

Our preliminary review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following potential approvability deficiencies:

1. 

2.

3.

4.

5.

6.

7. 

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

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

Sincerely,

*{See appended electronic signature page}*

James D. Vidra, Ph.D.  
Chemistry Team Leader for the Division of  
Anti-Infective and Ophthalmology Products  
DNDC Office of New Drug Chemistry  
Center for Drug Evaluation and Research

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/s/

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Jim Vidra

10/7/2005 12:58:41 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

**FILING COMMUNICATION**

NDA 50-809

Sicor Pharmaceuticals, Inc.  
Attention: Sonia Hernandez  
Manager, Regulatory Affairs  
19 Hughes  
Irvine, CA 92618

Dear Ms Hernandez:

Please refer to your July 29, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (azithromycin IV).

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act on October 1, 2005 in accordance with 21 CFR 314.101(a).

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

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

Sincerely,

*{See appended electronic signature page}*

Frances LeSane  
Chief Project Manager  
Division of Anti-Infective and  
Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

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/s/

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Carmen DeBellas  
9/29/2005 12:02:32 PM  
CSO

Carmen DeBellas  
9/29/2005 12:05:07 PM  
CSO



NDA 50-809

**NDA ACKNOWLEDGMENT**

Sicor Pharmaceuticals, Inc.  
Attention: Sonia Hernandez  
Manager, Regulatory Affairs  
19 Hughes  
Irvine, CA 92618

Dear Ms. Hernandez:

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

Name of Drug Product: Azithromycin for Injection  
Review Priority Classification: S  
Date of Application: July 29, 2005  
Date of Receipt: August 2, 2005  
Our Reference Number: NDA 50-809

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 October 1, 2005 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be June 2, 2006.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We are deferring submission of your pediatric studies until June 2, 2009. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of section 2 of the Pediatric Research Equity Act (PREA) within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Please cite the NDA number listed above 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

If you have any questions, call Carmen DeBellas, Regulatory Project Manager, at (301) 827-2125.

Sincerely,

*{See appended electronic signature page}*

Maureen P. Dillon-Parker  
Chief, Project Management Staff  
Division of Anti-Infective and  
Ophthalmology Products  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

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/s/

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Maureen Dillon-Parker  
9/3/2005 06:10:39 PM  
NDA 50-809 Ack Ltr



RECEIVED

AUG 02 2005

MEGA / CDER



19 Hughes  
Irvine, CA 92618  
Toll Free: 800.729.9991  
Telephone: 949.455.4700  
Fax: 949.855.8210  
www.sicor.com

July 29, 2005

Janice M. Soreth, M.D.  
Division of Anti-Infective Drug Products (DAIDP), ODE IV  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Central Documentation Room, 5901-B  
Ammendale Road  
Beltsville, MD 20705-1266

N-000

RE: Azithromycin for Injection  
500 mg/vial and 2.5 g/vial  
505(b)(2) NDA — 50-809

Dear Dr. Soreth:

SICOR Pharmaceuticals requests approval of the proposed drug, Azithromycin for Injection, 500 mg/vial and 2.5 g/vial, a parenteral preparation supplied as:

Strength	Total Drug Content	How Supplied
100 mg/mL	500 mg Azithromycin per single dose vial	10 vials per shelf pack
	2.5 g Azithromycin per pharmacy bulk package	individually packaged

SICOR's Azithromycin for Injection, offered in a single-dose vial at 500 mg/vial, is formulated using the same active pharmaceutical moiety and inactive ingredients, and offered in the same dosage form, strength, and route of administration as Pfizer's Zithromax®. Additionally, SICOR is proposing a pharmacy bulk, offered at 2.5 g/vial to be reconstitution to 100 mg/mL, the same concentration as Pfizer's Zithromax®. The pharmacy bulk is also formulated using the same active pharmaceutical moiety and inactive ingredients, and in the same dosage form and route of administration as Pfizer's Zithromax®. Once reconstituted as directed in the package insert, SICOR's drug products contain the same active pharmaceutical moiety and inactive ingredients in the same concentrations as Pfizer's Zithromax®. Therefore, no new clinical data is presented in support of our proposed drug products.

In accordance with 314.54(a)(1)(iii) and under Section 505(b)(2), we identify Pfizer's Zithromax® (azithromycin for injection) as the previously approved drug under NDA No. 50-733 for which FDA has made a finding of safety and effectiveness. The Agency letter received 30 August 2004 from Lillian Gavrilovich (Deputy Director, Office of Drug Evaluation IV, CDER, FDA) confirms that our proposed drug products qualify for a 505(b)(2) application (provided in **Module 1, Section 1.3.1**). A copy of the summary of data supporting registration of Zithromax® under NDA 50-733 (obtained from a search of CDER's website) is provided in **Module 2, Attachment 1**.

ORIGINAL

SICOR's proposed drug product is not for a new molecular entity that is an active ingredient or a new indication for a use. Such Section 505(b)(2) applications, as defined by the FD&C Act, are excluded from application fees.

Azithromycin for Injection will be packaged in \_\_\_\_\_ glass vials. The vials will be sealed with \_\_\_\_\_

The manufacturing processes and facility used to produce Azithromycin for Injection provide aseptic environment and conditions. Aseptic Fill Validation is provided in **Sections 3.2.P.3.3** and **3.2.P.3.5** in accordance with MAPP 5020.1, "Product Quality Microbiology Information in the Common Technical Document - Quality (CTD-Q)."

Six (6) stability lots of Azithromycin for Injection, three of each product configuration, were manufactured and data are presented in **Module 3** of this application.

Information has been included within the body of this NDA or by reference to DMF No. \_\_\_\_\_ that addresses chemistry comments made to PIND 67,798 in the letter dated August 30, 2004 from the Agency.

The application consists of seven (7) volumes and has been formatted in accordance with the ICH Common Technical Document. Copies are provided as follows:

- 1) Archival Copy - One (1) set bound in Blue Jackets
- 2) Review Copies - Two (2) sets bound in Red Jackets
- 3) Desk Copies  
Five (5) sets of Modules 1 & 2 - labeled "Modules 1 & 2 - Desk Copy"

A CD containing PDF and MS Word files, and an annotated comparison of the proposed package insert against Pfizer's Zithromax® label are provided in **Module 1** of the review copy (Red Jacket).

A true copy of this application, which was bound in Burgundy Jackets, has been submitted to the U.S. Food and Drug Administration of Irvine, California, District Office.

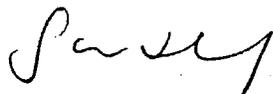
On July 2, 2003, we notified the Agency that Gensia Sicor Pharmaceuticals, Inc. changed the corporate company name to SICOR Pharmaceuticals, Inc. Please note we make this submission using the new corporate company name, SICOR Pharmaceuticals, Inc. Although we have initiated changes to documents revising the corporate company name to SICOR Pharmaceuticals,

Dr. Soreth  
July 29, 2005  
Page 3

Inc, there are still some documents in this submission with the previous company name, Gensia Sicor Pharmaceuticals, Inc.

We trust you will find the information in this application satisfactory for your review and approval. If there are any questions concerning this application, please do not hesitate in contacting me at (949) 455-4779. We can also be contacted by facsimile at (949) 583-7351.

Sincerely,



Sonia Hernandez  
Manager, Regulatory Affairs

cc: Mr. Alonza Cruse, District Director  
FDA, Los Angeles District  
19900 MacArthur Blvd., Suite 300  
Irvine, CA 92615