

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-089

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

<p>Richard Adams, Yanping Pan, and I called Debbie Jaskot at Teva regarding her request for a meeting to discuss Teva's application for Amoxicillin and Clavulanate Potassium for Oral Suspension.</p> <p>Debbie said the intent of the meeting would be to gain a better understanding of our issues so the firm could better prepare a complete response to the deficiency comments we sent. The firm proposes a — month expiration dating for the product and intends to make a commitment to revise the formulation or manufacturing process to improve stability. They said — month expiry could be justified based on fact that innovator has recently needed to decrease their shelf life to below 9 months.</p> <p>Mr. Adams said we agreed the innovator product appears to be having stability problems but that it appears to be a recent problem and that it appears previously to have had 2 year expiration dating. Also just because the innovator is having current problems, it does not appear to justify approving another product (Teva's) with known stability problems. He said OGD normally does not approve applications with less than 12 month dating. Ms. Jaskot said Teva may be able to propose — month dating. She said they were hoping we might be able to grant some flexibility in the lower assay limit on Clavulanate since it has an "indirect" efficacy in the product (i.e. no specific amount has been demonstrated to be needed in the formulation). Mr. Adams said since the USP has specifications they must be met</p> <p>Mr. Adams thus said we did not see the need for a meeting.</p> <p>Ms. Jaskot thanked us for the info but said her management may want to discuss further their request for a meeting. We indicated that is their prerogative</p> <p>This concluded the conversation.</p>	<p>DATE: 5/23/02</p>
	<p>ANDA NUMBER: 65-089</p>
	<p>PRODUCT NAME: Amox/Clav for Oral Suspension</p>
	<p>FIRM NAME: Teva Pharmaceuticals</p>
	<p>FIRM REPRESENTATIVE: Debbie Jaskot</p>
	<p>PHONE NUMBER: 215-285-6407</p>
<p>See also the attached memo prepared by Mr. Adams.</p> <p>V:\firmsnz\teva\telecons\65089.001</p>	<p>FDA REPRESENTATIVES: Richard Adams Yanping Pan Mark Anderson</p>
	<p>SIGNATURES:  Mark Anderson</p>

Redacted _____ / _____

5/23/02 TCON
ATTACHED MEMO

Page(s) of trade

secret and /or

confidential

commercial

information

MEMORANDUM

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

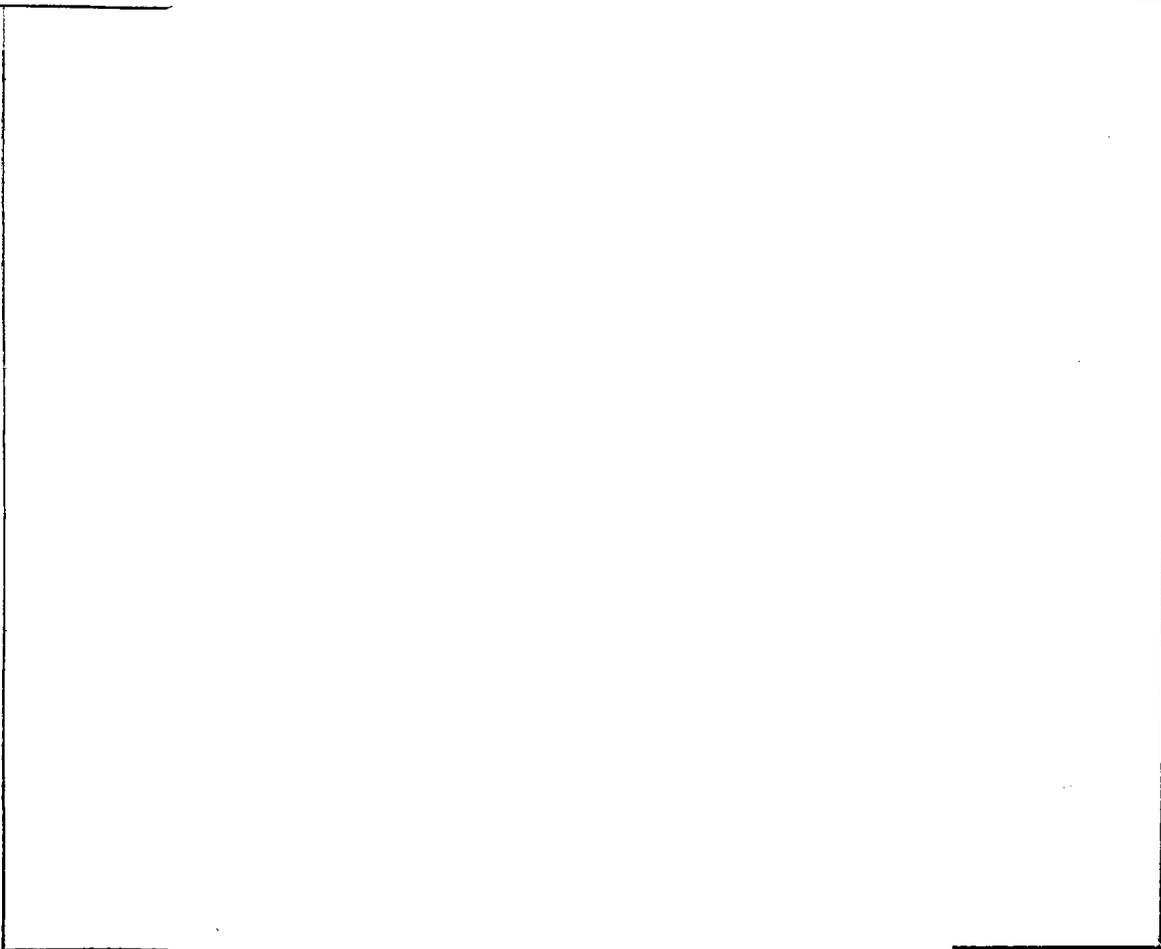
DATE: July 26, 2002

TO: ANDA 65-089 Amoxicillin /Clavulanate Potassium for Oral Suspension

FROM: R. C. Adams

SUBJECT: June 17, 2002 Amendment/Stability Data

This application was reviewed by Yanping Pan and found deficient on several counts, the most significant being failed stability data at several stations. The firm replied with an amendment submitted June 17, 2002 and included additional _____ stability data.



RECORD OF TELEPHONE CONVERSATION

<p>Richard Adams, Yanping Pan, and I called Vincent Andolina of Teva, to discuss the firm's amendment dated 2/28/03. Mr. Adams said that it appears that the data submitted on the new</p> <div style="border: 1px solid black; height: 300px; width: 100%;"></div> <p>Mr. Andolina acknowledged our comments and said he would look into the situation. He said the product, being a powder, made it more difficult to control but felt there were controls in place.</p> <p>V:\firmsnz\teva\telecons\65089.001</p>	DATE: 7/15/03
	ANDA NUMBER: 65-089
	PRODUCT NAME: Amoxicillin and Clavulanate Potassium for Oral Susp
	FIRM NAME: Teva Pharmaceuticals USA
	FIRM REPRESENTATIVE: Vincent Andolina
	PHONE NUMBER: 215-591-8642
	FDA REPRESENTATIVES: Richard Adams Yanping Pan Mark Anderson
	SIGNATURES:  Mark Anderson

M E M O R A N D U M

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

DATE: October 22, 2003

FROM: Chemistry Branch 6

SUBJECT: ANDA 65-089 - Amoxicillin and Clavulanate Potassium
for Oral Suspension USP, 200 mg/ 28.5 mg/5 mL, and 400
mg/57 mg/5 mL: Request for Change from Major to Minor
Amendment status

TO: The Record

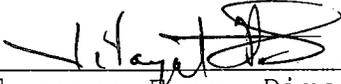
We issued a Major NA letter to TEVA on July 21, 2003 for their application for Amoxicillin and Clavulanate Potassium for Oral Suspension USP, based on the assumption that the firm would need to _____ due to inadequate stability data.

However, the firm has submitted an amendment dated October 3, 2003, which provides additional _____ stability data on their 100 mL package size (the only size presentation for which they are currently seeking approval) from the additional exhibit batches originally submitted in their 2/28/03 amendment which they feel supports a - -month expiry dating. The firm has not _____. Based on this it appears appropriate to reclassify the Major Amendment status to a Minor Amendment status. Upon review of the data, if they are not supportive, we will reissue a Major Not Approvable action.

Drafted by: M. Anderson, Project Manager/10/22/03

Through: Richard Adams, Team Leader/

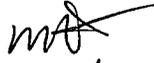
Concur:



Florence Fang, Director

Division of Chemistry II
Office of Generic Drugs

10/22/03.


R.C. Adams 10/22/03

RECORD OF TELEPHONE CONVERSATION

<p>Richard Adams, Yanping Pan, and I called Vincent Andolina at Teva. He was out of the office so we were referred to Jill Past.</p> <p>Mr. Adams explained that we need to have evidence to demonstrate that this drug product for oral suspension performs appropriately when constituted as per label directions, at release and on shelf life. Such evidence should include an evaluation of its suspendibility, a measure of its tendency to sediment, and, if warranted, a measure of its resuspendibility.</p> <p>We said the firm should describe the test they decide to use and describe whether the product sediments over time and provide a measure of how easily it is resuspended.</p> <p>The information can come in as a Telephone Amendment via FAX with hard copy to the file</p> <p>V:\firmsnz\teva\telecons\65089.004</p>	DATE: 3/26/04
	ANDA NUMBER: 65-089
	PRODUCT NAME: Amoxicillin and Clavulanate Potassium 200mg and 400 mg
	FIRM NAME: TEVA
	FIRM REPRESENTATIVE: Jill Past
	PHONE NUMBER: 215-591-8642
	FDA REPRESENTATIVES: Richard Adams Yanping Pan Mark Anderson
	SIGNATURES: Mark Anderson

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 65-089

CORRESPONDENCE

ANDA 65-089

TEVA Pharmaceuticals USA
Attention: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454
|||||

MAY 29 2001

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to the telephone conversation dated May 7, 2001 and your correspondence dated May 11, 2001.

NAME OF DRUG: Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg(base)per 5 mL and 400 mg/57 mg (base)per 5 mL

DATE OF APPLICATION: April 12, 2001

DATE (RECEIVED) ACCEPTABLE FOR FILING: April 13, 2001

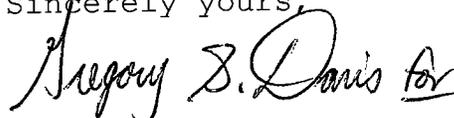
We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

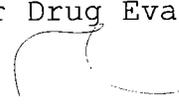
Should you have questions concerning this application, contact:

Mark Anderson
Project Manager
(301) 827-5848

Sincerely yours,



Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research



ANDA 65-089

cc: DUP/Jacket
Division File
Field Copy
HFD-610/R.West
HFD-610/P.Rickman
HFD-92
HFD-615/M.Bennett
HFD-600/
Endorsement:

HFD-615/GDavis, Chief, RSB *Davis 29-MAY-2001* date

HFD-615/BFritsch, CSO *BFritsch 5/24/01* date

Word File

V:\FIRMSnz/teva/ltrs&rev/65089.ack

F/T

ANDA Acknowledgment Letter!



Corporate Headquarters:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Phone: (215) 591 3000
FAX: (215) 591 8600

July 10, 2001

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

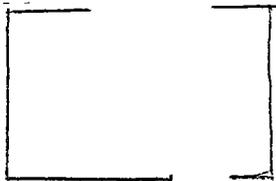
TELEPHONE AMENDMENT

NEW CORRESP

AND A # 65-119
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
200 mg/ 28.5 mg/ 5 ml and 400 mg/ 57 mg/ 5 ml
TELEPHONE AMENDMENT - RESPONSE TO JULY 6, 2001 REQUEST

Dear Mr. Buehler:

We submit herewith an amendment to the above-referenced abbreviated new drug application in response to a July 6, 2001 telephone conversation between Mark Anderson of the Office of Generic Drugs and Vincent Andolina of TEVA Pharmaceuticals USA. The following information is being provided per Mr. Anderson's request on clarification of the manufacturing site address of _____



Manufacturing Site:



Also, please find enclosed a revised cover page for Section VIII.1, which is intended to replace page 6058 of our original ANDA.

It is the belief of TEVA Pharmaceuticals USA that the above constitutes a complete response to the July 6, 2001 telephone request. We look forward to your continued review and approval of ANDA # 65-119. Should you have any questions regarding the information contained herein, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/dl
Enclosures



Corporate Headquarters:

TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

889
ANDA # 65-119

**AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
200 mg/ 28.5 mg/ 5 ml and 400 mg/ 57 mg/ 5 ml**

TELEPHONE AMENDMENT

In accord with the 21 CFR 314.96(b), TEVA Pharmaceuticals USA hereby certifies that the field copy is a true copy of the technical section of this submission and has been provided to the Division of Emergency Investigations Operations.

Vincent Andolina

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects



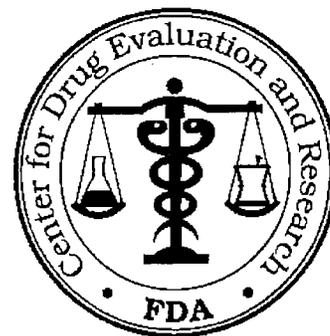
7/10/2001

MAJOR AMENDMENT

ANDA 65-089

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

OCT 24 2001



TO: APPLICANT: Teva Pharmaceuticals USA

TEL: 215-591-3000

ATTN: Vincent Andolina

FAX: 215-591-8812

FROM: Mark Anderson

PROJECT MANAGER: 301-827-5789

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated April 12, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg/5 mL and 400 mg/57 mg/5 mL.

Reference is also made to your amendment dated: July 10, 2001.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (6 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance

SPECIAL INSTRUCTIONS:

Chemistry comments are provided *also Labeling and Bioequivalence comments*

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

10/24/2001

FAX

ATTACHMENT

Redacted 3

Page(s) of trade

secret and /or

confidential

commercial

information



Administrative Offices:
 TEVA PHARMACEUTICALS USA
 1090 Horsham Road, PO Box 1090
 North Wales, PA 19454-1090

Deborah A. Jaskot, M.S., RAC
 Executive Director, Regulatory Affairs

Phone: (215) 591 3000
 FAX: (215) 591 8600

*Noted:
 to Richard Adam
 (fax copy) FYE*

May 3, 2002

Gary Buehler, Director
 Office of Generic Drugs
 Food and Drug Administration
 Document Control Room
 Metro Park North II
 7500 Standish Place, Room 150
 Rockville, MD 20855-2773

*WAE
 See T. com +
 memos
 dated
 5/23/02
 MA*

**NC
 NEW CORRESP**

ANDA #65-089
 AMOXICILLIN AND CLAVULANATE POTASSIUM for ORAL SUSPENSION,
 200 mg/ 28.5 mg/ 5 mL AND 400 mg/ 57 mg/ 5 mL

Dear Mr. Buehler:

Teva Pharmaceuticals USA seeks a meeting with key members of the staff of the Office of Generic Drugs with regard to the above pending ANDA. Teva has been working to address the issues raised in a major review letter issued October 24, 2001. However, due to the unique aspects of this product, we believe that a face-to-face meeting, primarily to share with office staff the knowledge that we have gained about the product from our efforts, would be beneficial to both the agency as well as applicants going forward.

As you are aware, the brand product, Augmentin POS, is formulated with overages of the labeled active ingredients. Through our testing of the brand product we have estimated what the formulation overages are and have sought to duplicate them. This process does involve some uncertainty and, given the stability profile for both the brand and the proposed generic product, we believe that we may not have taken full advantage of the extent of overage that we would be permitted to use. Additionally, the contribution of the clavulanate potassium to the efficacy of the product is atypical which raises questions about the appropriate specifications for this ingredient.

In light of these aspects of the development of this product, we believe that a face-to-face meeting is necessary to adequately present the information surrounding the issues. The details of our request are as listed below.

**RECEIVED
 MAY 06 2002
 OGD / CDER**

Date: May 13 – 31 inclusive

Office Attendees Requested:

Mr. Gary Buehler
Dr. Dale Conner
Mr. Bob West
Mr. Mark Anderson
Mr. Richard Adams
Review Chemist

Teva Attendees Proposed:

Ms. Deborah Jaskot
Dr. Paul Fackler
Mr. Jack Hoblitzell
Dr. Kurt Nielsen

A proposed agenda for the meeting is attached for your consideration. A data package will be prepared and provided to each of the Office attendees in advance of the meeting date once it is established.

Teva appreciates your consideration of this request and awaits your response.

Sincerely,



DAJ
Enclosure

Teva Pharmaceuticals USA
ANDA 65-089
Amoxicillin and Clavulanate Potassium for Oral Suspension

Scope of Meeting: This product is extremely difficult to formulate and has some unique characteristics which are not readily apparent in a typical ANDA presentation format. Prior to answering the outstanding major deficiency letter from October 24, 2001, we hope in this meeting to set forth an overview of the nature of this product and our development efforts to date in order to enhance the agency's understanding of the product's inherent difficulties. It is hoped that with this additional background, the agency's resources in the continuing review of this application can be optimized. We would also appreciate any information that the agency can offer to help in our efforts going forward with the understanding, of course, that any information provided is or would be available to any and all applicants equally.

Proposed Meeting Agenda

Introduction and Presentation of Goals

Deborah Jaskot – Executive Director, Regulatory Affairs

Development History and Comparisons to Brand Product Stability and Expiration Dating

Jack Hoblitzell – Director, Pharmaceutical R&D

Proposed Options for Teva's Product



Kurt Nielsen – Executive Director, Generic R&D

Discussion of Literature Regarding Plasma Concentrations of Clavulanic Acid, Impact of

Paul Fackler – Director, Biopharmaceutics

Discussion and Close



Administrative Offices:
 TEVA PHARMACEUTICALS USA
 1090 Horsham Road, PO Box 1090
 North Wales, PA 19454-1090

Vincent Andolina, RAC
 Director, Regulatory Affairs
 Liquids, Semisolids and Specialty Projects

Phone: (215) 591 3000
 FAX: (215) 591 8600

June 17, 2002

Gary Buehler, Director
 Office of Generic Drugs
 Food and Drug Administration
 Document Control Room
 Metro Park North II
 7500 Standish Place, Room 150
 Rockville, Maryland 20855-2773

*Labeling review
 drafted 10/30/03
 A. Vega
 N.B. was never documented
 as containing labeling fill
 10/03 av*

MAJOR AMENDMENT

ORG AMENDMENT

N/A

ANDA # 65-089
 AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
 200 mg/ 28.5 mg/ 5 mL and 400 mg/ 57 mg/ 5 mL
 MAJOR AMENDMENT – RESPONSE TO OCTOBER 24, 2001 REVIEW LETTER

Dear Mr. Buehler:

We submit herewith a Major Amendment to the above-referenced pending abbreviated new drug application in response to your October 24, 2001 review letter. Reference is also being made to a telephone conversation between Rob Vincent of TEVA Pharmaceuticals USA and Krista Scardina of the Office of Generic Drugs, Division of Bioequivalence on April 29, 2002. For ease of your review, a copy of the review letter is provided in **Attachment 1**. Comments are addressed in the order in which they were presented.

I. Chemistry:

1.

2.

RECEIVED

JUN 18 2002

OGD / CDER

6/17/2002
CORRESPONDENCE

Redacted

6

Page(s) of trade

secret and /or

confidential

commercial

information

ANDA # 65-089

Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/ 28.5 mg/ 5 mL and 400 mg/ 57 mg/ 5 mL

Major Amendment – Response to October 24, 2001 Review Letter

Page 8 of 8

It is the belief of TEVA Pharmaceuticals USA that the above constitutes a complete response to the October 24, 2001 review letter. We look forward to your continued review and approval of ANDA # 65-089. Should you have any questions regarding the information contained herein, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/dl

Enclosures

**APPEARS THIS WAY
ON ORIGINAL**

MAJOR AMENDMENT

ANDA 65-089

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



AUG 20 2002

TO: APPLICANT: Teva Pharmaceuticals USA

TEL: 215-591-8642

ATTN: Vincent Andolina

FAX: 215-591-8812

FROM: Mark Anderson

PROJECT MANAGER: 301-827-5789

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated April 12, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg/5 mL and 400 mg/57 mg/5 mL.

Reference is also made to your amendment dated: June 17, 2002.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (1 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

Chemistry comments are provided. Labeling comments, if any, will be provided separately when the review is completed.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

AUG 20 2002

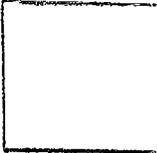
38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 65-089

APPLICANT: TEVA Pharmaceuticals USA

DRUG PRODUCT: Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg/5 mL and 400 mg/57 mg/5 mL

The deficiency presented below represent MAJOR deficiency.



Sincerely yours,

fs

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL



*Labeling review
drafted 10/30/03
A. Vezza*

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Phone: (215) 591 8642
FAX: (215) 591 8812

February 28, 2003

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

MAJOR AMENDMENT

ORIG AMENDMENT
N/A/C

ANDA # 65-089
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
200 mg/ 28.5 mg/ 5 mL and 400 mg/ 57 mg/ 5 mL
MAJOR AMENDMENT – RESPONSE TO AUGUST 20, 2002 REVIEW LETTER

Dear Mr. Buehler:

We submit herewith a Major Amendment to the above-referenced pending ANDA in response to your August 20, 2002 review letter. For ease of your review, a copy of the letter is provided in **Attachment 1**. Per your recommendation,



herein.

RECEIVED
MAR 03 2003
OGD / CDER

Redacted 2

2/28/2003
CORRESPONDENCE

Page(s) of trade

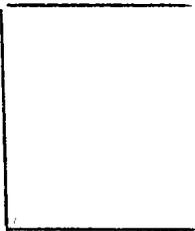
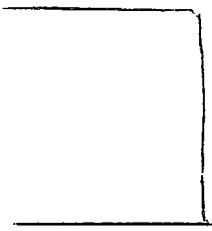
secret and /or

confidential

commercial

information

Attachment 10:

- 
- 
- 

Attachment 11:

- Draft package insert labeling and comparison to the previous version

It is the belief of TEVA Pharmaceuticals USA that the above constitutes a complete response to a request for additional exhibit batches made in your August 20, 2002 review letter. We look forward to your continued review and approval of ANDA # 65-089. Should you have any questions regarding the information contained herein, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vivian Andolina

VA/dl

Enclosures

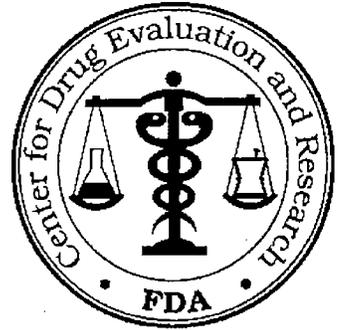
**APPEARS THIS WAY
ON ORIGINAL**

MAJOR AMENDMENT

ANDA 65-089

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

JUL 21 2003



APPLICANT: TEVA Pharmaceuticals USA

TEL: 215-591-8642

ATTN: Vincent Andolina

FAX: 215-591-8812

FROM: Mark Anderson

PROJECT MANAGER: 301-827-5737

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated April 12, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg (base)/5 mL and 400 mg/57 mg (base)/5 mL.

Reference is also made to your amendment(s) dated: February 28, 2003.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (1 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

MA

JUL 21 2003

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

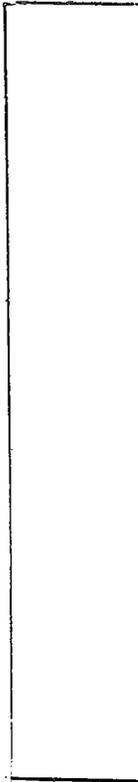
ANDA: 65-089

APPLICANT: TEVA Pharmaceuticals USA

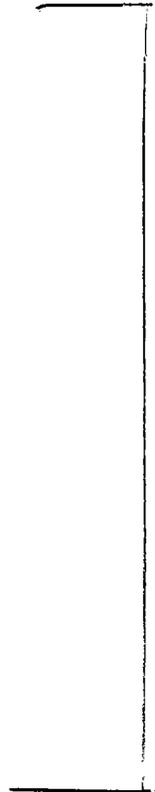
DRUG PRODUCT: Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg (base)/5 mL and 400 mg/57 mg (base)/5 mL

The deficiencies presented below represent Major deficiencies.

1.



2.



3.

Sincerely yours,



Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research



Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Direct Dial: (215) 591 8642
Direct FAX: (215) 591 8812
vincent.andolina@tevausa.com

October 3, 2003

ORIG AMENDMENT

N/A

~~MAJOR AMENDMENT~~

Minor

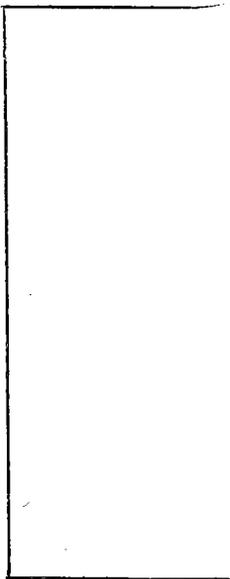
Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ANDA # 65-089
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
200 mg/ 28.5 mg per 5 mL and 400 mg/ 57 mg per 5 mL
MAJOR AMENDMENT – RESPONSE TO JULY 21, 2003 REVIEW LETTER

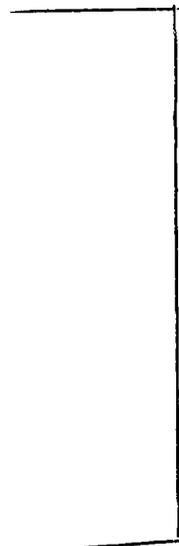
Dear Mr. Buehler:

We submit herewith a Major Amendment to the above-referenced pending ANDA in response to the July 21, 2003 review letter. Reference is also made to our June 17, 2002 and February 28, 2003 amendments to this file. For ease of your review, a copy of the July 21, 2003 letter is provided in **Attachment 1**. Comments are addressed in the order in which they were presented.

1.



2.



RECEIVED

OCT 06 2003

CGD/CDLR

Redacted 2

10/3/2003
CORRESPONDENCE

Page(s) of trade

secret and /or

confidential

commercial

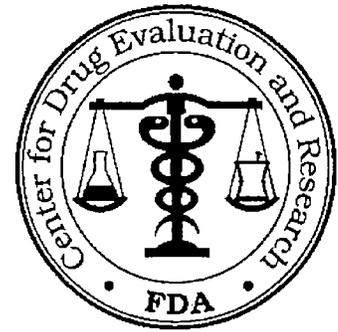
information

MINOR AMENDMENT

ANDA 65-089

DEC 18 2003

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



APPLICANT: TEVA Pharmaceuticals USA

TEL: 215.591.8642

ATTN: Vincent Andolina

FAX: 215.591.8812

FROM: Mark Anderson

PROJECT MANAGER: (301) 827-5737

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated April 12, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg/5 mL and 400 mg/57 mg/5 mL.

Reference is also made to your amendment dated: October 3, 2003.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (1 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments are provided. We also await receipt of labeling amendment in response to labeling deficiencies faxed to you on 11/7/03

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

KA

DEC 18 2003

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

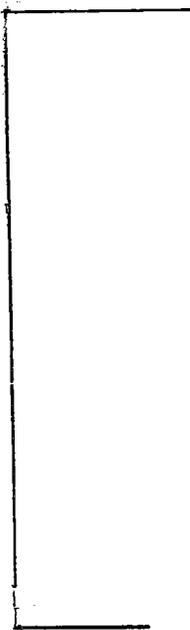
ANDA: 65-089

APPLICANT: TEVA Pharmaceuticals USA

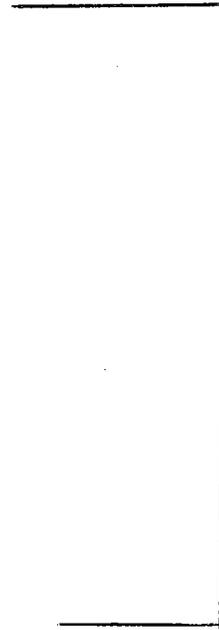
DRUG PRODUCT: Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/28.5 mg (base)/5 mL and 400 mg/57 mg (base)/5 mL

The deficiencies presented below represent Minor Amendment deficiencies. Note: these comments were previously issued on November 12, 2003 as a Telephone Amendment request. Due to the delay in responding, they are being reissued as Minor Amendment deficiencies.

1.



2.



3.

Sincerely yours,

R.C. Adams for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs



Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Phone: (215) 591 8642
FAX: (215) 591 8812

February 24, 2004

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

MINOR AND LABELING AMENDMENT

ORIG AMENDMENT

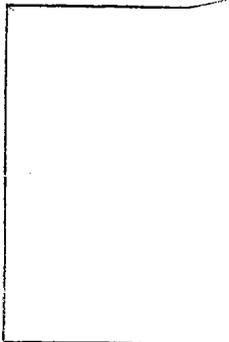
al/HM

ANDA # 65-089
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
200 mg/ 28.5 mg per 5 mL and 400 mg/ 57 mg per 5 mL
MINOR AND LABELING AMENDMENT – RESPONSE TO DECEMBER 18, 2003
CMC REVIEW LETTER AND NOVEMBER 7, 2003 LABELING REVIEW LETTER

Dear Mr. Buehler:

We submit herewith a Minor Amendment to the above-referenced pending ANDA in response to the December 18, 2003 CMC review letter and November 7, 2003 review letter from the Labeling Review Branch, OGD. For ease of your review, copies of both letters are provided in **Attachment 1**. Comments are addressed in the order in which they were presented.

Please refer to our telephone communication of January 8, 2004 with Mark Anderson, R.Ph., Project Manager, Richard Adams, Chemistry Team Leader; Susan Zuk, Ph.D., review chemist; and Yanping Pan, Ph.D., review chemist. Mr. Adams stated that the Office of Generic Drugs



FEB 25 2004

OGD/REG AFFAIRS

I. Chemistry, Manufacturing and Controls:

1.

2.

3.



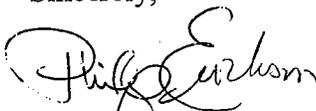
II. Labeling

Provided in **Attachment 6**, please find twelve copies of final print container labels for the 100 mL reconstituted suspension package size as well as a comparison to the previous version, which have been revised in accord with the recommendations made in the November 7, 2003 review letter from the Labeling Review Branch.

The requested revisions have also been incorporated into the revised package insert as well as the correction of the typographical error in the volume of water required for reconstitution. Twelve copies of final print package insert along with a comparison to the previous version are provided in **Attachment 7**.

It is the belief of TEVA Pharmaceuticals USA that the above constitutes a complete response to your December 18, 2003 CMC review letter and November 7, 2003 Labeling review letter. We look forward to your continued review and approval of ANDA # 65-089. Should you have any questions regarding the information contained herein, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

 for VA

VA/dl
Enclosures

RECEIVED
FEB 25 2004



4-1

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Phone: (215) 591 8642
FAX: (215) 591 8812

April 2, 2004

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

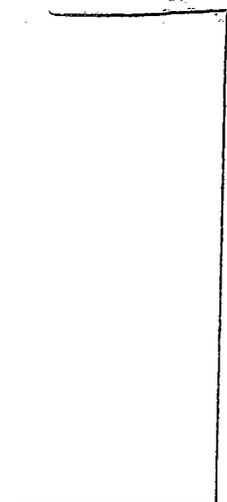
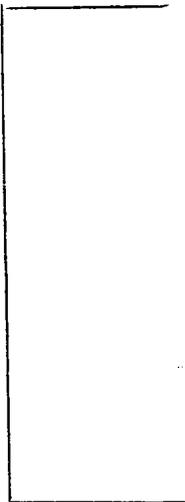
TELEPHONE AMENDMENT

ORIG AMENDMENT
N/AM

ANDA # 65-089
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION
USP, 200 mg/ 28.5 mg per 5 mL and 400 mg/ 57 mg per 5 mL
TELEPHONE AMENDMENT – RESPONSE TO MARCH 25, 2004 REQUEST

Dear Mr. Buehler:

We submit herewith a Telephone Amendment to the above-referenced pending ANDA in response to the March 25, 2004 telephone conversation between Mark Anderson, Richard Adams and Yanping Pan of the Office of Generic Drugs and Jill Pastore of Teva Pharmaceuticals USA. Specifically, a request was made to measure the tendency of our product to form sediment from reconstituted suspension and estimate the amount of effort required to resuspend the sediment.



ED

APR 05 2004

OGD/ODR

ANDA # 65-089

*Amoxicillin and Clavulanate Potassium For Oral Suspension USP, 200 mg/ 28.5 mg per 5 mL and
400 mg/ 57 mg per 5 mL*

Telephone Amendment – Response to March 25, 2004 request

Page 2 of 2

the product release requirements. Therefore, no changes have been made to the actual Finished Product Procedure Manual. A copy is however, provided herein for completeness of the file.

It is the belief of Teva Pharmaceuticals USA that the above constitutes a complete response to your office's March 25, 2004 telephone request. We look forward to your continued review and approval of ANDA # 65-089.

Sincerely,



VA/dl

Enclosures

**APPEARS THIS WAY
ON ORIGINAL**

ORIGINAL



Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Direct Dial: (215) 591 8642
Direct FAX: (215) 591 8812
vincent.andolina@tevausa.com

April 23, 2004

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

LABELING AMENDMENT

ORIG AMENDMENT
N/A

ANDA # 65-089
AMOXICILLIN AND CLAVULANATE POTASSIUM FOR ORAL SUSPENSION USP,
200 mg/ 28.5 mg per 5 mL and 400 mg/ 57 mg per 5 mL
LABELING AMENDMENT – RESPONSE TO MARCH 26, 2004 LABELING REVIEW
LETTER

Dear Mr. Buehler:

We submit herewith a Labeling Amendment to the above-referenced pending ANDA in response to the March 26, 2004 review letter from the Labeling Review Branch. For ease of your review, a copy of the letter is provided in **Attachment 1**. Your comments are addressed in the order in which they were presented.

RECEIVED

APR 26 2004

OGD/CDER

1. CONTAINER:

Provided in **Attachment 2**, please find 12 copies of final print container labels, which have been revised in accord with your recommendations. A comparison to the previous version is also provided in this attachment.

2. INSERT:

Regarding comment 2.a.i., please note that our labeling is consistent with the labeling for the reference-listed drug with regard to inclusion of the strengths of the active ingredients throughout the text. Additionally, please note that the paragraph noted in comment 2.f. has not been incorporated into our labeling since Teva's formulation of Amoxicillin and Clavulanate Potassium for Oral Suspension USP contains both mannitol and aspartame inactive ingredients. Thus, the information pertaining to the difference in diarrhea profiles attributed to the presence of these ingredients in chewable tablets versus oral suspension is specific to the innovator's formulation. All other recommendations have been incorporated into our revised package insert. Twelve copies of the updated final print package insert along with a comparison to the previous version are provided in **Attachment 3**.

ANDA # 65-089

Amoxicillin and Clavulanate Potassium for Oral Suspension USP, 200 mg/ 28.5 mg per 5 mL and
400 mg/ 57 mg per 5 mL

Labeling Amendment – Response to March 26, 2004 Review Letter

Page 2 of 2

It is the belief of TEVA Pharmaceuticals USA that the above constitutes a complete response to your March 26, 2004 Labeling review letter. We look forward to your final approval of ANDA # 65-089. Should you have any questions regarding the information contained herein, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Narciso Andolina

VA/dl

Enclosures

**APPEARS THIS WAY
ON ORIGINAL**