

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75-761

CORRESPONDENCE

February 10, 2000

Greg Davis
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP

NC
OK to file!
505(w)(2)(A) OK
2/18/00 [Signature]

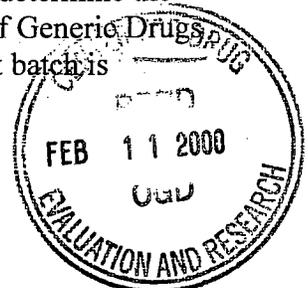
**Re: Amiodarone Hydrochloride Injection
50 mg/mL , ANDA 75-761
3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY
Number of Volumes: 1 Volume**

AMENDMENT TO ORIGINAL ANDA

Dear Mr. Davis,

In response to our telephone conversation on Tuesday, February 1, 2000 for the Amiodarone Hydrochloride Injection Abbreviated New Drug Application # 75-761, the following items have been addressed:

1. Addition of the Reference Listed Drug to the 356h form.
2. _____ revised DMF referral letter authorizing the Food and Drug Administration to access _____ DMF on APP's behalf.
3. A universal cGMP statement for American Pharmaceutical Partners, Inc.
4. Revised pages to state the theoretical yield as _____. It should be known that some instances remained at _____. However, the following footnote has been added to explain the _____ quantity:
_____ is the actual volume packaged and is used to determine the maximum commercial batch size as per the Office of Generic Drugs, Drug Guide #22-90. The Theoretical Yield for the exhibit batch is _____.



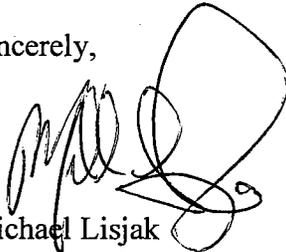
5. — Validation Data was inadvertently omitted in the original correspondence. I have updated and included the appropriate paginated pages for Section XXII.

I have enclosed the corrected and additional pages for both the Archival and Review copies in one correspondence.

Furthermore, in compliance with 21 CFR 314.94(d)(5), a true and complete copy (the Field Copy) of this abbreviated application is being provided to Ms. Brenda J. Holman, District Director, Buffalo District, Food and Drug Administration, 300 Pearl Street, HFR-NE300, Buffalo, NY 14202. We certify that the field copy is a true and complete copy of this amendment to the Abbreviated New Drug Application.

If you have any additional questions or concerns, please do not hesitate to contact the undersigned at (708) 547-2365 or Nancy Bauer, Associate Director, Regulatory Affairs at (708) 547-2381.

Sincerely,



Michael Lisjak
Regulatory Scientist

**APPEARS THIS WAY
ON ORIGINAL**

ANDA 75-761

American Pharmaceutical Partners, Inc.
Attention: Michael Lisjak
2045 North Cornell Avenue
Melrose Park, IL 60160
|||||.....|||||

FEB 18

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 February 1, 2000 and your correspondence dated February 10, 2000.

NAME OF DRUG: Amiodarone Hydrochloride Injection, 50 mg/mL,
3 mL vials

DATE OF APPLICATION: December 22, 1999

DATE (RECEIVED) ACCEPTABLE FOR FILING: December 23, 1999

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.

**APPEARS THIS WAY
ON ORIGINAL**

Should you have questions concerning this application, contact:

Tim Ames
Project Manager
(301) 827-5849

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Robert L. West".

Robert L. West, M.S., R.Ph.
Director

Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

August 8, 2000

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP
NC

Re: Amiodarone Hydrochloride Injection
50 mg/mL
3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY

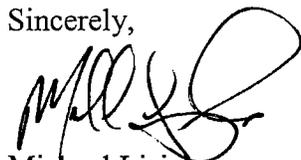
INTENT TO FILE AN AMENDMENT

Dear Mr. Buehler:

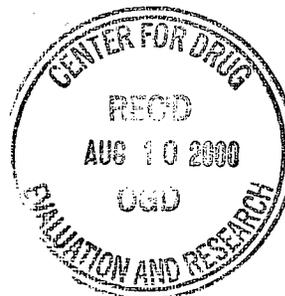
Reference is made to our December 22, 1999 submission of an Abbreviated New Drug Application (ANDA) for Amiodarone Hydrochloride Injection, ANDA # 75-761. Reference is also made to the June 21, 2000 Major Deficiency to this application. In accordance with 21 CFR 314.120(a)(1), American Pharmaceutical Partners, Inc. is informing you of our **intent to file an amendment** in response to this communication.

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned at (708) 547-2365 or Nancy Bauer, Associate Director, Regulatory Affairs at (708) 547-2381.

Sincerely,



Michael Lisjak
Regulatory Scientist



November 10, 2000

*Labeling review
drafted 1/24/01
A. Vezza*

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AC

Re: Amiodarone Hydrochloride Injection
50 mg/mL
3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY
Number of Volumes: 1 Volume

MAJOR AMENDMENT
Chemistry and Microbiology Deficiencies

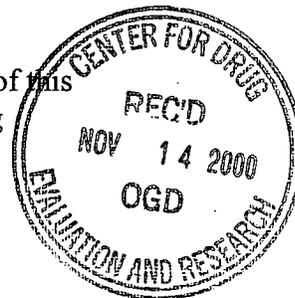
Dear Mr. Buehler:

Reference is made to our December 22, 1999 submission of an Abbreviated New Drug Application (ANDA) for Amiodarone Hydrochloride Injection, ANDA # 75-761. Reference is also made to the attached June 21, 2000 Major Chemistry Deficiency and to the November 1, 2000 Microbiology Deficiency to this application, which are provided immediately after this letter.

American Pharmaceutical Partners, Inc. (APP) is submitting this amendment in response to each of the comments made in your communications dated June 21, 2000 and November 1, 2000. For ease of review, each of the reviewer's observation is provided in bold, followed by APP's response. Final Printed Labeling (FPL) is included in this response along with a separate binder containing twelve (12) copies of the FPL.

In accordance with 21 CFR 314.96(b), we hereby certify that a true and complete field copy of this supplement is being provided to the Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60606.

In addition, we hereby certify that a true and complete courtesy field copy of this supplement is being provided to the Buffalo District Office, Food and Drug Administration, 300 Pearle Street, HFR-NE300, Buffalo, NY 14202.

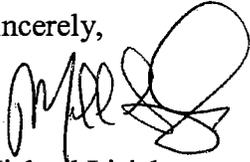


November 10, 2000

Page 2

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned at (708) 547-2365 or Mitchall Clark, Vice President, Regulatory Affairs at (708) 547-3618.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael Lisjak". The signature is stylized with a large, looping initial "M" and a trailing flourish.

Michael Lisjak
Senior Regulatory Scientist

**APPEARS THIS WAY
ON ORIGINAL**

April 10, 2001

ARCHIVAL

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

*labeling review
drafted 4/16/01
A. Vezza*

ORIG AMENDMENT

N/A

**Re: ANDA 75-761
Amiodarone Hydrochloride Injection
50 mg/mL
3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY
Number of Volumes: 1 Volume**

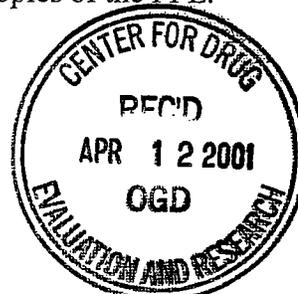
LABELING AMENDMENT

Dear Mr. Buehler:

Reference is made to our December 22, 1999 original submission of an Abbreviated New Drug Application (ANDA) for Amiodarone Hydrochloride Injection, ANDA # 75-761. Reference is also made to our November 13, 2000 response to the Food and Drug Administration's June 21, 2000 Major Chemistry Deficiency and to the November 1, 2000 Microbiology Deficiency to this application.

Further reference is made to a January 29, 2001 telephone call from Mr. Adolph Vezza, Labeling Review Branch, FDA, regarding APP's Final Printed Labeling submitted in the November 13, 2000 Major Amendment. Mr. Vezza instructed APP to add a single use vial statement to the container (vial) label and a similar statement to the carton (ex. 10 single vials).

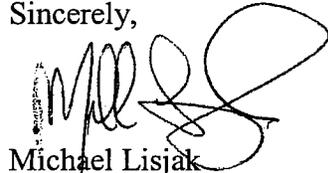
In response to Mr. Vezza's request, Final Printed Labeling (FPL) is included in **Attachment 1**. Annotated side-by-side comparison of APP's November 13, 2000 labeling to the proposed labeling is included in **Attachment 2**. Also included in this response, is a separate binder containing twelve (12) copies of the FPL.



April 10, 2001
Page 2

Should you have any questions or require additional information concerning this amendment, please do not hesitate to contact the undersigned at (708) 547-2365 or Dale Carlson, Associate Director, Regulatory Affairs at (708) 547-2336.

Sincerely,

A handwritten signature in black ink, appearing to read 'ML' followed by a large, stylized flourish.

Michael Lisjak
Senior Regulatory Scientist

**APPEARS THIS WAY
ON ORIGINAL**

May 4, 2001

ARCHIVAL

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

ORIG. AMENDMENT

N/AA

Re: **ANDA 75-761**
Amiodarone Hydrochloride Injection
50 mg/mL
3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY
Number of Volumes: 1 Volume

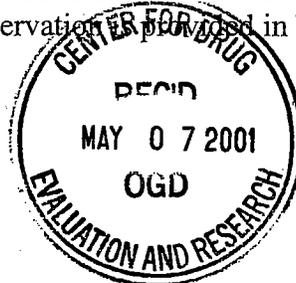
TELEPHONE AMENDMENT
Chemistry Deficiencies

Dear Mr. Buehler:

Reference is made to American Pharmaceutical Partners, Inc.'s (APP) December 22, 1999 submission of an Abbreviated New Drug Application (ANDA) for Amiodarone Hydrochloride Injection, ANDA # 75-761. Reference is also made to a November 10, 2000 major amendment to the Amiodarone ANDA.

Further reference is made to an April 24, 2001 telephone conversation between Jeen Min, FDA, Ed Ramos, FDA, Michael Lisjak, APP, Pearle Torralba, APP, and Dale Carlson, APP. The teleconference was to discuss APP's November 10, 2000 major amendment to the Amiodarone ANDA. In the discussion, Mr. Ramos indicated that there were three (3) deficient items, which could be responded to via a telephone amendment. In addition to the three (3) items noted from the teleconference, APP is also updating its raw material specification by tightening the limits for Bacterial Endotoxin to be consistent with the microbiological method validation provided in the original submission.

American Pharmaceutical Partners, Inc. (APP) is submitting this telephone amendment in response to each of the comments made in the teleconference dated April 24, 2001. For ease of review, each of the reviewer's observations are provided in bold, followed by APP's response.



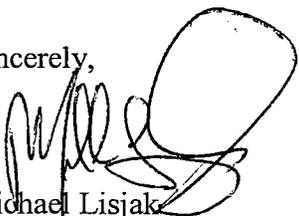
May 4, 2001
Page 2

In accordance with 21 CFR 314.96(b), we hereby certify that a true and complete field copy of this amendment is being provided to the Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60606.

In addition, we hereby certify that a true and complete courtesy field copy of this amendment is being provided to the Buffalo District Office, Food and Drug Administration, 300 Pearle Street, HFR-NE300, Buffalo, NY 14202.

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned at (708) 547-2365 or Dale Carlson, Associate Director, Regulatory Affairs at (708) 547-2373.

Sincerely,



Michael Lisjak
Senior Regulatory Scientist

**APPEARS THIS WAY
ON ORIGINAL**

June 19, 2001

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

N/A/S
ORIG AMENDMENT
ARCHIVAL

Re: ANDA 75-761
Amiodarone Hydrochloride Injection
50 mg/mL
3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY
Number of Volumes: 1 Volume

Response to Microbiology Deficiencies

Dear Mr. Buehler:

Reference is made to our December 22, 1999 submission of an Abbreviated New Drug Application (ANDA) for Amiodarone Hydrochloride Injection, ANDA # 75-761. Reference is also made to our November 10, 2000 response to the June 21, 2000 Major Chemistry Deficiency and to the November 1, 2000 Microbiology Deficiency to this application.

Further reference is made to the June 12, 2001 Microbiology Deficiency to this application, which is provided immediately after this letter.

American Pharmaceutical Partners is submitting this Amendment in response to the comment made in your communication dated June 12, 2001. For ease of review, the reviewer's observation is provided in bold, followed by APP's response.

In accordance with 21 CFR 314.96(b), we hereby certify that a true and complete field copy of this Amendment is being provided to the Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60606.

In addition, we hereby certify that a true and complete courtesy field copy of this Amendment is being provided to the Buffalo District Office, Food and Drug Administration, 300 Pearle Street, HFR-NE300, Buffalo, NY 14202.



June 19, 2001

Page 2

Should you have any questions or require additional information concerning this submission, please do not hesitate to contact the undersigned at (708) 547-2365 or Dale Carlson, Associate Director of Regulatory Affairs at (708) 547-2373.

Sincerely,



Michael Lisjak
Senior Regulatory Scientist

APPEARS THIS WAY
ON ORIGINAL



Labeling review
drafted 6/18/02
A. Neza

May 21, 2002

Noted
S. Thompson
5/22/02

NIAM

ORIG AMENDMENT

ARCHIVAL FPL

Gary Buehler, Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

Re: **ANDA 75-761**
Amiodarone Hydrochloride Injection
50 mg/mL, 3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY

**MINOR AMENDMENT TO AN ORIGINAL ANDA
FINAL APPROVAL REQUESTED**

Dear Mr. Buehler:

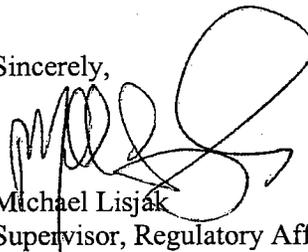
Reference is made to our Abbreviated New Drug Application (ANDA 75-761) for Amiodarone Hydrochloride Injection submitted December 22, 1999. Reference is also made to the attached August 23, 2001 tentative approval letter received for this ANDA.

As described in the tentative approval letter, American Pharmaceutical Partners (APP) hereby submits this minor amendment to inform the Agency that APP has no updated information to submit for ANDA 75-761, with the exception of updated labeling due to changes in the innovator's labeling (Wyeth-Ayerst, Cordarone®). Final Printed Labeling (FPL) is included in **Attachment 1** and an annotated side-by-side comparison of APP's final printed labeling to APP's tentatively approved labeling (current labeling) is included in **Attachment 2**. In addition, APP is providing twelve (12) copies of the FPL in the FDA review copy.

Furthermore, in compliance with 21 CFR 314.96 (b), a true and complete copy (the Field Copy) of this amendment is being provided to Arlyn Baumgarten, Director, Chicago District, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, Chicago, Illinois 60606. We certify that the Field Copy is a true and complete copy of this submission. Additionally, a courtesy field copy of this amendment is being forwarded to the Buffalo District Office.

Should you have any questions or require additional information concerning this submission, please do not hesitate to contact the undersigned at (708) 486-2063 or Dale Carlson, Associate Director, Regulatory Affairs, at (708) 486-2071.

Sincerely,


Michael Lisjak
Supervisor, Regulatory Affairs

RECEIVED

MAY 22 2002

OGD / CDER

Handwritten initials and date: M/L, 5/22/02

3.1

July 2, 2002

*Labeling review
drafted 7/15/02
A. Vezza*

ORIG AMENDMENT

N/AF

Gary Buehler, Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

ARCHIVAL

**Re: ANDA 75-761
Amiodarone Hydrochloride Injection
50 mg/mL, 3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY**

LABELING AMENDMENT

Dear Mr. Buehler:

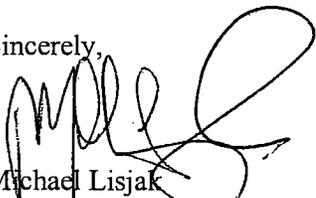
Reference is made to our Abbreviated New Drug Application (ANDA 75-761) for Amiodarone Hydrochloride Injection submitted December 22, 1999.

Further reference is made to the attached June 19, 2002 labeling deficiency letter from Mr. Adolph Vezza, Labeling Review Branch, FDA, regarding APP's Final Printed Labeling submitted in our minor amendment for the Request for Final Approval submitted May 21, 2002.

In response to the FDA deficiencies, Final Printed Labeling (FPL) is included in **Attachment 1**. It should be known that only the insert has been updated in this response. In regards to deficiency 1, Carton, Add "25 vials" to the carton labeling, this statement is heat stamped directly on the carton label during the packaging process. Therefore, the Final Printed Labeling submitted in our May 21, 2002 minor amendment is current. An annotated side-by-side comparison of APP's May 21, 2002 labeling to APP's proposed labeling is included in **Attachment 2**. In addition, APP is providing twelve (12) copies of the FPL in the FDA review copy.

Should you have any questions or require additional information concerning this submission, please do not hesitate to contact the undersigned at (708) 486-2063 or Dale Carlson, Associate Director, Regulatory Affairs, at (708) 486-2071.

Sincerely,


Michael Lisjak
Supervisor, Regulatory Affairs

RECEIVED

JUL 03 2002

OGD / CDER

July 22, 2002

*Labeling review
drafted 7/30/02
A. Vezza*

Gary Buehler, Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

ARCHIVAL

ORIG AMENDMENT

N/AF

FPL

**Re: ANDA 75-761
Amiodarone Hydrochloride Injection
50 mg/mL, 3 mL fill in a 3 mL vial (Code 601603)
Manufacturing Site: Grand Island, NY**

LABELING AMENDMENT

Dear Mr. Buehler:

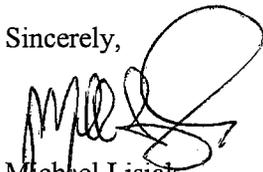
Reference is made to our Abbreviated New Drug Application (ANDA 75-761) for Amiodarone Hydrochloride Injection submitted December 22, 1999.

Further reference is made to the attached July 16, 2002 labeling deficiency letter from Mr. Adolph Vezza, Labeling Review Branch, FDA, regarding APP's Final Printed Labeling submitted in our labeling amendment submitted July 2, 2002.

In response to the FDA deficiencies, Final Printed Labeling (FPL) is included in **Attachment 1**. An annotated side-by-side comparison of APP's July 2, 2002 labeling (Current Labeling) to APP's proposed labeling is included in **Attachment 2**. In addition, APP is providing twelve (12) copies of the FPL in the FDA review copy.

Should you have any questions or require additional information concerning this submission, please do not hesitate to contact the undersigned at (708) 486-2063 or Dale Carlson, Associate Director, Regulatory Affairs, at (708) 486-2071.

Sincerely,



Michael Lisjak
Supervisor, Regulatory Affairs

RECEIVED

JUL 23 2002

OGD / CDER