

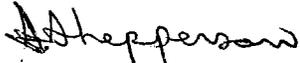
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-458

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

<p>The firm was contacted regarding the following items related to ANDA 76-458:</p> <ol style="list-style-type: none"> 1. The limits for _____ in the Drug Substance need to be tightened to be in conformance with the data provided, regarding _____ . The Agency referred to the February 10, 2003 amendment, Lot 1100009. Most of the solvents have a limit of _____ 2. The specifications for finished product need to be tightened. The firm will need to tighten the individual unknown specification to NMT —% at release and stability. The USP specification for any individual impurity is NMT 0.4%. 3. The firm is using USP reference standards and has been requested to send qualifying data. 	<p style="text-align: center;">DATE:</p> <p style="text-align: center;">06-APR-2004</p> <hr/> <p style="text-align: center;">ANDA NUMBER</p> <p style="text-align: center;">76-458</p> <hr/> <p style="text-align: center;">TELECON INITIATED BY AGENCY</p> <hr/> <p style="text-align: center;">PRODUCT NAME:</p> <p style="text-align: center;">Fluoxetine Oral Solution, 20 mg/5 mL</p> <hr/> <p style="text-align: center;">FIRM NAME:</p> <p style="text-align: center;">Par Pharmaceutical, Inc.</p> <hr/> <p style="text-align: center;">FIRM REPRESENTATIVES:</p> <p style="text-align: center;">Julie Szozda</p> <hr/> <p style="text-align: center;">TELEPHONE NUMBER:</p> <p style="text-align: center;">201-802-4131</p> <hr/> <p style="text-align: center;">FDA REPRESENTATIVES</p> <p style="text-align: center;">U.Venkataram, PHD L.Tang, PHD</p> <hr/> <p style="text-align: center;">SIGNATURES:</p> <p style="text-align: center;"></p>
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Orig: ANDA 76-458

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-458

CORRESPONDENCE

Par
Pharmaceutical,
Inc.



One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

July 15, 2002

Copy 1
Copy 2
Copy 3 (field)*

Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2
7500 Standish Place, Room 150
Rockville, Maryland 20855

**RE: FLUOXETINE ORAL SOLUTION, USP
EQ 20 MG BASE PER 5 ML**

Dear Sir or Madam:

We herewith submit, in duplicate, an abbreviated new drug application for Fluoxetine Oral Solution, USP 20 mg/5 mL. The application is submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

The official name of the drug relied upon as the basis upon which this application may be filed is fluoxetine hydrochloride. The proprietary name of said drug is Prozac®. A copy of the appropriate pages of the Approved Drug Products with Therapeutic Equivalence Evaluations List is enclosed in SECTION II to show that the proposed drug is the same as the listed drug.

The certification concerning the patent is set forth under SECTION III. The approved insert labeling for the listed drug is enclosed in SECTION V. The third (field) copy certification is provided in SECTION XXI.

Par Pharmaceutical, Inc. hereby requests a waiver of the *in-vivo* bioequivalence study requirements for Fluoxetine Oral Solution, USP 20 mg/5 mL, based on its therapeutic equivalence code designation of "AA" which indicates that there are no known or suspected bioequivalence problems associated with the product. Our waiver request and relevant formulation data are provided in SECTION VI.

RECEIVED

JUL 17 2002

OGD / CDER



FLUOXETINE ORAL SOLUTION, USP
EQ 20 MG PER 5 ML

FDA/CDER/OGD
July 15, 2002
Page 2 of 2 Pages

Please contact us if we may offer any assistance in your review of this application.

Very truly yours,
PAR PHARMACEUTICAL, INC.

A handwritten signature in cursive script that reads "Michelle Bonomi-Huvala".

Michelle Bonomi-Huvala
Senior Director, Regulatory Affairs/R&D
Enclosures

* Jerome G. Woysner
District Director
Food and Drug Administration
New York District Office
158-15 Liberty Avenue
Jamaica, New York 11433



**Par
Pharmaceutical,
Inc.**

One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

Copy 1
Copy 2 (archive)
Copy 3 (field)*

September 10, 2002

Via Facsimile (301-594-1174) and Overnight Mail

Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2
7500 Standish Place, Room 150
Rockville, Maryland 20855

**RE: ANDA 76-458, FLUOXETINE ORAL SOLUTION, USP
EQ 20 MG BASE PER 5 ML**

AMENDMENT

Dear Staff:

Reference is made to our abbreviated new drug application dated July 15, 2002 for Fluoxetine Oral Solution, USP EQ 20 mg Base per 5 mL. Reference is also made to telephone conversations of August 30 and September 10, 2002 with Mr. Martin Shimer of OGD, pertaining thereto.

In accordance with the above, Par Pharmaceutical, Inc. herewith withdraws the Paragraph III Certification for Patent Number 4,626,549.

In addition, Par is providing the following information in accordance with Mr. Shimer's August 30th request:

- A more legible copy of the supplier's Certificate of Analysis for Benzoic Acid, USP (manufacturer lot # 07010720-1, Par lot # 029376).
- Correspondence dated August 30, 2002 confirming submission by the manufacturer, _____ via facsimile of the quantitative and qualitative breakdown for _____ Natural Peppermint Extract _____ and _____ Artificial Sweet Cream Flavor. Please note that receipt of this information was confirmed by Martin Shimer during our September 10th telephone conversation.

A hard copy of this facsimile will be forwarded to Document Control.

We certify that the field copy is a true copy of the technical information contained in the archival and review copies of this amendment and was submitted to the New York District Office.

NEW CORRESP

NC

Addressed. NAI
12-SEP-2002
Judy L Davis

RECEIVED

SEP 11 2002

OGD / CDER



ANDA 76-458, FLUOXETINE ORAL SOLUTION, USP
EQ 20 MG BASE PER 5 ML

FDA/CDER/OGD
September 10, 2002
Page 2 of 2 Pages

This concludes our amendment to ANDA 76-458 for Fluoxetine Oral Solution, USP. If you have any questions or require additional information regarding the above matter, please do not hesitate to contact us.

Sincerely,
PAR PHARMACEUTICAL, INC.

A handwritten signature in cursive script that reads "Janis A. Picurro".

Janis A. Picurro
Product Manager, Regulatory Affairs/R&D
/encl.

* Jerome G. Woysner
District Director
Food and Drug Administration
New York District Office
158-15 Liberty Avenue
Jamaica, New York 11433

ANDA 76-458

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 *[Signature]* 12-SEP-2002 date
HFD-615/MShimer, CSO *[Signature]* date 12 September 2002
Word File V:\Firmsnz\Par\Ltrs&rev\76458.ack
F/T
ANDA Acknowledgment Letter!

MINOR AMENDMENT

ANDA 76-458

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)

DEC 12 2002



TO: APPLICANT: Par Pharmaceutical, Inc.

TEL: 845-425-7100

ATTN: Michelle Bonomi-Huvala

FAX: 845-425-6105

FROM: Stanley Shepperson

PROJECT MANAGER: 301-827-5798

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated July 15, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluoxetine Oral Solution USP, 20 mg (base)/5 mL.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (2 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. 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 you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

CMC comments included.

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.

AA 12/12/02

Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

12/12/2002 FDA FAX

Par
Pharmaceutical,
Inc.



One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

RECEIVED
N/AM.

Copy 1 ✓
Copy 2
Copy 3 (field)*

January 13, 2003

Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation and Research
Mcire Park North II
7500 Standish Place
Rockville, Maryland 20855

MINOR AMENDMENT

RE: Fluoxetine Oral Solution, USP 20 mg (base)/5mL
ANDA 76-458

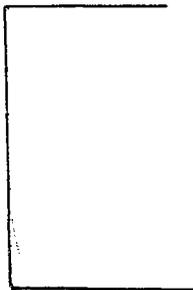
Dear Staff.

Dear Staff.

Reference is made to the Agency's minor amendment facsimile dated December 12, 2002 which outlines deficiencies relating to our abbreviated new drug application dated July 15, 2002 for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL. A photostatic copy of the Agency's December 12th correspondence is appended in Attachment I.

Par Pharmaceutical, Inc. is addressing the Agency's deficiencies with this minor amendment to ANDA 76-458. The Agency's comments and our responses follow.

Comment 1



7/11
1-23-03

RECEIVED

JAN 14 2003

OGD / CDER

Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

1/13/2003 PAR LETTER



**Par
Pharmaceutical,
Inc.**

One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

ORIGINAL AMENDMENT
N/A

Copy 1
Copy 2
Copy 3 (field)*

February 10, 2003

Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North II
7500 Standish Place
Rockville, Maryland 20855

ADDENDUM TO MINOR AMENDMENT

**RE: Fluoxetine Oral Solution, USP 20 mg (base)/5mL
ANDA 76-458**

Dear Staff:

Reference is made to the Agency's minor amendment facsimile dated December 12, 2002 relative to our abbreviated new drug application dated July 15, 2002 for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL. Reference is also made to our minor amendment dated January 13, 2003 which responded to the Agency's deficiencies. A photostatic copy of Par's minor amendment letter is appended in Attachment I for reference.

Please note that we are submitting an addendum to our minor amendment to include revised



We certify that the field copy is a true copy of the technical information contained in the archival and review copies of this addendum to our minor amendment of January 13th and was submitted to the New York District Office.

RECEIVED
FEB 11 2003
OGD / CDER



Fluoxetine Oral Solution, USP 20 mg (base)/5 mL
ANDA 76-458

FDA/CDER/OGD
February 10, 2003
Page 2 of 2 Pages

This concludes the addendum to the minor amendment for our abbreviated new drug application for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL, ANDA 76-458. If you have any questions regarding the above, please do not hesitate to contact us.

Sincerely,
PAR PHARMACEUTICAL, INC.

A handwritten signature in cursive script that reads "Janis A. Picurro".

Janis A. Picurro
Manager, Regulatory Affairs R&D
/encl.

* Jerome G. Woysner
District Director
Food and Drug Administration
New York District Office
158-15 Liberty Avenue
Jamaica, New York 11433



**Par
Pharmaceutical,
Inc.**

One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

ORIG AMENDMENT

N/AF

Copy 1
Copy 2

November 19, 2003

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2
7500 Standish Place, Room 150
Rockville, Maryland 20855

LABELING AMENDMENT

RE: ANDA #76-458, Fluoxetine Oral Solution, USP 20 mg (base)/5 mL

Dear Sir/Madam:

Reference is made to the October 29, 2003 e-mail from Adolph Vezza, Labeling Review Branch, of the FDA regarding the current generic labeling for the Fluoxetine products. A photostatic copy of Mr. Vezza's e-mail to Janis Picurro at Par Pharmaceutical together with the current labeling model is appended in Attachment I.

In support of this labeling amendment, we provide the following information:

Our package insert has been revised based on the current labeling model provided by Adolph Vezza of the FDA on October 29, 2003. Twelve (12) final printed copies of the revised package insert are enclosed in Attachment II.

In accordance with 21 CFR 314.94(a)(8)(iv) and to facilitate review, a side-by-side comparison of the package insert with our July 15, 2002 submission, with all differences annotated and explained, is provided in Attachment III.

Eli Lilly and Company is entitled to a period of marketing exclusivity for I-362 (for the treatment of panic disorder with or without agoraphobia) which expires July 29, 2005. Par Pharmaceutical does not intend to label its drug product for this indication until exclusivity expires. An updated exclusivity statement is enclosed in Attachment IV.

In addition, the container labels for this product have been revised to add an equivalent statement for fluid ounces to the package size. Twelve (12) final printed copies of the updated container labels are enclosed in Attachment V. A side by side comparison of the container labels with our original submission, with all differences annotated and explained, is also provided in this section.

This concludes the labeling amendment to our abbreviated new drug application for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL, ANDA 76-458. If you have any questions regarding the above, please do not hesitate to contact us.

Sincerely,

Par Pharmaceutical, Inc.

Julie Szozda

Senior Associate, Regulatory Affairs R&D

Enclosure

RECEIVED

NOV 21 2003

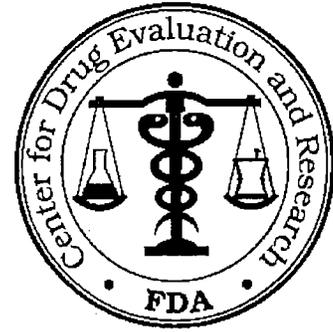
03/11/03

MINOR AMENDMENT

ANDA 76-458

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)

DEC 22 2003



APPLICANT: Par Pharmaceutical, Inc.

TEL: 201-802-4131

ATTN: Julie Szozda

FAX: 201-391-3106

FROM: Stanley Shepperson

PROJECT MANAGER: (301) 827-5798

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated July 15, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluoxetine Oral Solution USP, 20 mg/5 mL.

Reference is also made to your amendment(s) dated: January 13, February 10 and November 19, 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. 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 you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

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.

JWA
12/22/03

DEC 22 2003

36. Chemistry Comments to be Provided to the Applicant

ANDA: 76-458

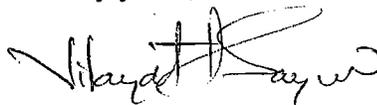
APPLICANT: Par Pharmaceutical, Inc.

DRUG PRODUCT: Fluoxetine Oral Solution USP, 20 mg(base)/5 mL

The deficiency presented below represents a MINOR deficiency:

The Division of Chemistry has no further comments regarding the Chemistry, Manufacturing and Controls (CMC) issues. However, Labeling is deficient and the deficiencies were communicated to you on December 18, 2003. It is necessary that all the Labeling deficiencies be corrected before the approval of this application. We may request additional data, if necessary.

Sincerely yours,



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

Par
Pharmaceutical,
Inc.



Copy 1 ✓
Copy 2

One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

December 31, 2003

ORIG AMENDMENT

N/AF

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2
7500 Standish Place, Room 150
Rockville, Maryland 20855

MINOR AMENDMENT

RE: ANDA #76-458, Fluoxetine Oral Solution, USP 20 mg (base)/5 mL

Dear Sir/Madam:

Reference is made to the Agency's facsimiles of December 18, 2003 and December 22, 2003 (copies appended in Attachment I) as well as our November 19, 2003 labeling amendment for the Fluoxetine products.

In support of this minor amendment, we provide the following information:

The exclusivity statement has been updated to include Eli Lilly and Company's period of marketing exclusivity for the New Patient Population (NPP) exclusivity [patients 6 to 11 years old] which expires July 3, 2006 [extended due to pediatric exclusivity]. Par Pharmaceutical does not intend to label its drug product for this indication until exclusivity expires. The updated exclusivity statement is enclosed in Attachment II.

Par Pharmaceutical, Inc. herewith withdraws the Paragraph III Certification for the '549 patent and its associated use code U-154 [treatment of animals suffering from an appetite disorder]. Please note, method of use statement (Section VIII) was submitted with the original application which addresses the use code (U-154). *

The package insert has been revised in accordance with the labeling provided by Adolph Vezza of the FDA on December 18, 2003. Twelve (12) final printed copies of the revised package insert are enclosed in Attachment III. In accordance with 21 CFR 314.94(a)(8)(iv) and to facilitate review, a side-by-side comparison of the package insert with our November 19, 2003 submission, with all differences annotated and explained, is provided in Attachment IV.

In addition, the container labels for this product have been updated to reflect the change in the storage temperature in accordance with the Agency's recommendation. Twelve (12) final printed copies of the updated container labels are enclosed in Attachment V.

This completes the minor amendment to our abbreviated new drug application for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL, ANDA 76-458. If you have any questions regarding the above, please do not hesitate to contact us.

Sincerely,

Par Pharmaceutical, Inc.

Julie Szozda

Senior Associate, Regulatory Affairs R&D

Enclosure

RECEIVED

JAN 02 2004

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**Par
Pharmaceutical,
Inc.**



One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

Copy 1 ✓
Copy 2

January 28, 2004

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2
7500 Standish Place, Room 150
Rockville, Maryland 20855

**ORIG AMENDMENT
N/AF
FPL**

LABELING AMENDMENT

RE: ANDA #76-458, Fluoxetine Oral Solution, USP 20 mg (base)/5 mL

Dear Sir/Madam:

Reference is made to the January 16, 2004 telephone conversation with Adolph Veza of the Labeling Review Branch regarding our December 31, 2003 minor amendment which provided for revised labeling for the Fluoxetine products.

Our package insert has been updated based on the January 16, 2004 telephone conversation with the Agency. Twelve (12) final printed copies of the revised package insert are enclosed in Attachment I.

In accordance with 21 CFR 314.94(a)(8)(iv) and to facilitate review, a side-by-side comparison of the package insert with our December 31, 2003 submission, with all differences annotated and explained, is provided in Attachment II.

This completes the labeling amendment to our abbreviated new drug application for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL, ANDA 76-458. If you have any questions regarding the above, please do not hesitate to contact us.

Sincerely,

Par Pharmaceutical, Inc.

Julie Szozda
Senior Associate, Regulatory Affairs R&D

Enclosure

**RECEIVED
JAN 30 2004
OGD/CL**



**Par
Pharmaceutical,
Inc.**

One Ram Ridge Road, Spring Valley, NY 10977
(845) 425-7100 • Fax (845) 425-7907

Copy 1
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ORIG AMENDMENT

Am

April 28, 2004

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2
7500 Standish Place, Room 150
Rockville, Maryland 20855

TELEPHONE AMENDMENT

RE: ANDA #76-458, Fluoxetine Oral Solution, USP 20 mg (base)/5 mL

Dear Sir/Madam:

Reference is made to the Agency's telephone call of April 6, 2004 requesting that the raw material and finished product specifications be revised for Fluoxetine Oral Solution.

In support of this telephone amendment, we provide the following information:

Comment 1

To conform with data provided for lot #11000091, _____

Response

Comment 2

Revise the finished product specifications/procedures for Fluoxetine Oral Solution to include any unknown impurities of NMT \leq % for release and stability.

RECEIVED

APR 29 2004

CGD/CDER



Fluoxetine Oral Solution, USP 20 mg (base)/5 mL

April 28, 2004

Page 2

Response

In accordance with the Agency's recommendation, the finished product/stability monograph (F/S-699-005) was revised to include "Any Unknown Impurity" of NMT — 6 for release and stability. In addition, "Any Individual Impurity" was changed to read "Any Known Impurity". The revised finished product/stability monograph is appended in Attachment II.

This completes the telephone amendment to our abbreviated new drug application for Fluoxetine Oral Solution, USP 20 mg (base)/5 mL, ANDA 76-458. If you have any questions regarding the above, please do not hesitate to contact us.

Sincerely,

Par Pharmaceutical, Inc.

A handwritten signature in cursive script that reads "Julie Szozda".

Julie Szozda

Senior Associate, Regulatory Affairs R&D

Enclosure

Jerome G. Woyshner, District Director
New York District
Food and Drug Administration
158-15 Liberty Avenue
Jamaica, NY 11433