DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 075525

LABELING ORDER

Hi-Tech Pharmacal Co., Inc.
369 Bayview Ave.
Amityville, NY 11701

Attention: Joanne Curri
Director of Regulatory Affairs

Dear Ms. Curri:

Please refer to your Abbreviated New Drug Application (ANDA) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Fluoxetine Oral Solution, USP.

On May 12, 2014, we sent you a letter invoking our authority under section 505(o)(4) of the FDCA to require safety related label changes to the labeling of fluoxetine oral solution to address postmarketing reports in the FDA Adverse Event Reporting System (FAERS) and biomedical literature that suggest an association between the use of antidepressants and angle-closure glaucoma. The decision to require safety labeling changes was based on new safety information about this risk identified since this product was approved. You were directed to submit, within 30 days of the date of that letter, a supplement proposing changes to the approved labeling, or notify FDA that you do not believe a labeling change is warranted, and submit a statement detailing the reasons why such a change is not warranted.

On June 17, 2014, you also received a follow-up email to inquire about your intent to submit a labeling supplement as requested. You were also advised that requirements under section 505(o)(4) of the Act apply to NDAs, BLAs, and ANDAs without a currently marketed reference listed drug under an NDA, unless approval of your application has been withdrawn in the Federal Register. Therefore, even if you are not currently marketing your product, because your application has not been withdrawn, you are required to comply with the safety labeling change requirements in section 505(o)(4) of the Act.

The 30 days have passed and we have not received any submission from you addressing our letter dated May 12, 2014.

You failed to respond to our May 12, 2014, letter within 30 days and have therefore forfeited the discussion period. Under the authority of Section 505(o)(4)(E), we are ordering you to make all of the changes in the labeling listed in the May 12, 2014, letter (attached).

Pursuant to Section 505(o)(4)(E), a changes being effected (CBE) supplement containing all of the changes to the labeling that are listed in the May 12, 2014, letter must be received by FDA by August 6, 2014, for Fluoxetine Oral Solution, USP.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

Alternatively, by July 27, 2014, you may appeal this Order using the Agency's established formal dispute resolution process as described in 21 CFR 10.75 and the Guidance for Industry, "Formal Dispute Resolution: Appeals Above the Division Level." http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM343101.pdf. The appeal should be submitted as a correspondence to your ANDA referenced above. Identify the submission as "**Formal Dispute Resolution Request**" both on the cover letter and on the outside envelope. A copy of the submission should be sent to:

Amy Bertha
CDER Formal Dispute Resolution Project Manager
Food and Drug Administration
Building 22, Room 6465
10903 New Hampshire Avenue
Silver Spring, MD 20993

In addition, to expedite coordination of any such appeal, a copy of the submission should also be sent to:

Kyle Snyder
Labeling Project Manager
Office of Generic Drugs
Food and Drug Administration
Bldg. 75, Room 3660
10903 New Hampshire Avenue
Silver Spring, MD 20993

Refer to the Guidance for Industry, "Formal Dispute Resolution: Appeals Above the Division Level" for further instruction regarding the content and format of your request. Questions regarding the formal dispute resolution process may be directed to Amy Bertha, CDER Formal Dispute Resolution Project Manager, at (301) 796-1647. Appeals received by the Agency later than July 27, 2014, will not be entertained.

Failure to respond to this Order within the specified timeframes is a violation of section 505(o)(4) of the FDCA and could subject you to civil monetary penalties under section 303(f)(4) of the FDCA, 21 U.S.C. 333(f)(4), in the amount of up to $250,000 per violation, with additional penalties if the violation continues uncorrected. Further, such a violation would cause your product to be misbranded under section 502(z) of the Act, 21 U.S.C. 352(z), which could subject

you to additional enforcement actions, included but not limited to seizure of your product and injunction.

If you have any questions, contact Andrew Kim, Regulatory Project Manager, at (240) 402-8983 or andrew.kim@fda.hhs.gov.

Sincerely,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

ENCLOSURE: Safety Labeling Change Notification Letter

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 075525

SAFETY LABELING CHANGE NOTIFICATION

Hi-Tech Pharmacal Co., Inc.
369 Bayview Ave.
Amityville, NY 11701

Attention: Joanne Curri
Director of Regulatory Affairs

Dear Ms. Curri:

Please refer to your Abbreviated New Drug Application (ANDA) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Fluoxetine Oral Solution, USP.

Section 505(o)(4) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to make safety related label changes based upon new safety information that becomes available after approval of the drug or biological product.

Since Fluoxetine Oral Solution, USP was originally approved, we have become aware of postmarketing reports in the FDA Adverse Event Reporting System (FAERS) and biomedical literature that suggest and association between the use of antidepressants and angle-closure glaucoma. We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

In accordance with section 505(o)(4) of the FDCA, we are notifying you that based on the new safety information described above, we believe that the new safety information should be included in the labeling for antidepressants as follows:

HIGHLIGHTS OF PRESCRIBING INFORMATION
[Note: The Highlights RECENT MAJOR CHANGE follows the black box WARNING:]

---------- RECENT MAJOR CHANGE ----------

Warnings and Precautions (5.X) MM/20XX [Note: your date of implementation]

[Note: The Highlights bullet follows Potential for Cognitive and Motor Impairment bullet]

----------WARNINGS AND PRECAUTIONS----------

- *Angle- Closure Glaucoma: Angle closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants. (5.X)*

FULL PRESCRIBING INFORMATION: CONTENTS

5 WARNINGS AND PRECAUTIONS
[Note: Place 5.X Angle Closure Glaucoma after Potential for Cognitive and Motor Impairment]

5.X *Angle- Closure Glaucoma*

17 PATIENT COUNSELING INFORMATION
[Note: Place 17.X Angle-Closure Glaucoma after Potential for Cognitive and Motor Impairment]

17.X *Angle- Closure Glaucoma*

FULL PRESCRIBING INFORMATION

5 WARNINGS AND PRECAUTIONS
[Note: Place 5.X below Potential for Cognitive and Motor Impairment]

5.X Angle Closure Glaucoma
Angle-Closure Glaucoma: The pupillary dilation that occurs following use of many antidepressant drugs including [Note: Add your product name here]_____ may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy.

6 ADVERSE REACTIONS
6.X Postmarketing Experience
[Note- If applicable, please make the following change]
[Any listing of glaucoma under Adverse Reactions should be changed to specify "angle-closure glaucoma". Listing of increased intraocular pressure as an adverse reaction may continue.]

17 PATIENT COUNSELING INFORMATION
[Note: Place after Potential for Cognitive and Motor Impairment]

17.X Angle Closure Glaucoma

Patients should be advised that taking [Note: Add your product name here] _____ can cause mild pupillary dilation, which in susceptible individuals, can lead to an episode of angle- closure glaucoma. Pre-existing glaucoma is almost always open-angle glaucoma

because angle- closure glaucoma, when diagnosed, can be treated definitively with iridectomy. Open-angle glaucoma is not a risk factor for angle- closure glaucoma. Patients may wish to be examined to determine whether they are susceptible to angle-closure, and have a prophylactic procedure (e.g., iridectomy), if they are susceptible. [see Warnings and Precautions (5.X)]

MEDICATION GUIDE

[Note: Place text as the last numbered X, after numbers 1-3, and X will follow " Call a healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:"]

X. Visual problems:

- *eye pain*
- *changes in vision*
- *swelling or redness in or around the eye*

Only some people are at risk for these problems. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are.

Except for retaining any current listing of increased intraocular pressure under adverse reactions in the label, please remove all information on open angle glaucoma or increased intraocular pressure or a history of either conditions from the label and Medication Guide since angle closure glaucoma is distinct from these conditions, and they are not known risk factors for angle closure glaucoma.

In accordance with section 505(o)(4), within 30 days of the date of this letter, you must submit a supplement proposing changes to the approved labeling in accordance with the above direction, or notify FDA that you do not believe a labeling change is warranted and submit a rebuttal statement detailing the reasons why such a change is not warranted. If you submit a supplement that includes only language identical to that specified above, the supplement may be submitted as a changes being effected (CBE-0) supplement. If the supplement includes proposed language that differs from that above, submit a prior approval supplement (PAS).

Requirements under section 505(o)(4) apply to NDAs, BLAs, and ANDAs without a currently marketed reference listed drug approved under an NDA, including discontinued products, unless approval of an application has been withdrawn in the Federal Register. Therefore, the requirements described in this letter apply to you, unless approval of your application has been withdrawn in the Federal Register.

Under section 502(z), failure to submit a response in 30 days may subject you to enforcement action, including civil money penalties under section 303(f)(4)(A) and an order to make whatever labeling changes FDA deems appropriate to address the new safety information.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

SAFETY LABELING CHANGES UNDER 505(o)(4) - PRIOR APPROVAL SUPPLEMENT

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – REBUTTAL (CHANGE NOT WARRANTED)."

Prominently identify subsequent submissions related to the safety labeling changes supplement with the following wording in bold capital letters at the top of the first page of the submission:

SUPPLEMENT XXX
SAFETY LABELING CHANGES UNDER 505(o)(4) - AMENDMENT

Please submit your response electronically. If you have any questions, contact Kyle Snyder, Labeling Project Manager, at (240) 276-8997 or kyle.snyder@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Kathleen Uhl, M.D.
Acting Director
Office of Generic Drugs
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.

/s/

ROBERT L WEST
05/12/2014
Deputy Director, Office of Generic Drugs, for
Kathleen Uhl, M.D.

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

/s/

JULIE M CALL
07/22/2014
Originally signed by Dr. Throckmorton for Dr. Woodcock.