

Appendix 1: Questions from PTSD instruments

DAVIDSON SELF-RATING PTSD SCALE:

IN THE PAST WEEK, HOW MUCH TROUBLE HAVE YOU HAD WITH THE FOLLOWING SYMPTOMS?

ANSWER QUESTIONS BASED ON THE FOLLOWING SCALE:

FREQUENCY:

0 = Not at all

1 = Once only

2 = 2-3 times

3 = 4-6 times

4 = Everyday

SEVERITY:

0 = Not at all Distressing

1 = Minimally Distressing

2 = Moderately Distressing

3 = Markedly Distressing

4 = Extremely Distressing

DAVIDSON SELF-RATING PTSD SCALE:

1. Have you had painful images, memories or thoughts of the event?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

2. Have you had distressing dreams of the event?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

3. Have you felt as though the event was reoccurring? Was it as if you were reliving it?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

4. Have you been upset by something which reminded you of the event?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

5. Have you been avoiding any thoughts or feelings about the event?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

6. Have you been avoiding doing things or going into situations which remind you of the event?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

7. Have you found yourself unable to recall important parts of the event?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

8. Have you had difficulty enjoying things?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

9. Have you felt distant or cut-off from other people?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

10. Have you been unable to have sad or loving feelings or have you generally felt numb?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

11. Have you found it hard to imagine having a long life span fulfilling your goals?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

12. Have you had trouble falling asleep or staying asleep?

FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

13. Have you been irritable or had outbursts of anger?  
FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

DAVIDSON SELF-RATING PTSD SCALE:

14. Have you had difficulty concentrating?  
FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

15. Have you felt on edge, been easily distracted, or had to stay "on guard"?  
FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

16. Have you been jumpy or easily startled?  
FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

17. Have you been physically upset by reminders of the event? (this includes sweating, trembling, racing heart, shortness of breath, nausea, diarrhea)  
FREQUENCY: \_ (0-4) SEVERITY: \_ (0-4)

IMPACT OF EVENT SCALE FOR PTSD:

THE SUBJECT SHOULD BE INSTRUCTED TO RATE HIS/HER EXPERIENCE OF THE FOLLOWING ITEMS ON A FOUR POINT SCALE OF INTENSITY:

0=Not At All  
1=Mild  
3=Moderate  
5=Severe

Event :

IMPACT OF EVENT SCALE FOR PTSD

INTRUSION ITEMS:

1. I had waves of strong feelings about it. (0,1,3,5)
2. Things I saw or heard suddenly reminded me of it. (0,1,3,5)
3. I thought about it when I didn't mean to. (0,1,3,5)
4. Images related to it popped into my mind. (0,1,3,5)
5. Any reminder brought back emotions related to it. (0,1,3,5)
6. I have difficulty falling asleep because of images or thoughts related to the event. (0,1,3,5)
7. I have bad dreams related to the event. (0,1,3,5)

KEY: 0=Not At All, 1=Mild, 3=Moderate, 5=Severe

AVOIDANCE ITEMS:

1. I knew that a lot of unresolved feelings were still there, but I kept them under wraps. (0,1,3,5)
2. I avoided letting myself get emotional when I thought about it or was reminded of it. (0,1,3,5)

3. I wished to banish it from my store of memories. (0,1,3,5)

4. I made an effort to avoid talking about it. (0,1,3,5)  
IMPACT OF EVENT SCALE FOR PTSD

AVOIDANCE ITEMS:

5. I felt unrealistic about it, as if it hadn't happened or as if it wasn't real. (0,1,3,5)

6. I stayed away from things or situations that might remind me of it. (0,1,3,5)

7. My emotions related to it were kind of numb. (0,1,3,5)

8. I didn't let myself have thoughts related to it. (0,1,3,5)

KEY: 0=Not At All, 1=Mild, 3=Moderate, 5=Severe

CLINICIAN-ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

A. THE TRAUMATIC EVENT:

REMINDER: A FREQUENCY RATING OF 0 INDICATES THAT THE INTENSITY IS 0 ALSO.

CLINICIAN-ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

B. THE TRAUMATIC EVENT IS PERSISTENTLY REEXPERIENCED:

(1) RECURRENT AND INTRUSIVE RECOLLECTIONS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(2) DISTRESS WHEN EXPOSED TO EVENTS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(3) ACTING OR FEELING AS IF EVENT RECURRING

Frequency: \_ (0-4) Intensity: \_ (0-4)

(4) RECURRENT DISTRESSING DREAMS OF EVENT

Frequency: \_ (0-4) Intensity: \_ (0-4)

CLINICIAN-ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

REEXPERIENCING INTENSITY AND FREQUENCY SUMS

Frequency: \_ (0-16) Intensity: \_ (0-16)

REEXPERIENCING INTENSITY AND FREQUENCY MEANS

Frequency: (0-4) Intensity: (0-4)

CLINICIAN ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

C. PERSISTENT AVOIDANCE OF STIMULI/NUMBING OF RESPONSIVENESS:

(5) EFFORTS TO AVOID THOUGHTS OR FEELINGS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(6) EFFORTS TO AVOID ACTIVITIES OR SITUATIONS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(7) INABILITY TO RECALL TRAUMA ASPECTS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(8) MARKEDLY DIMINISHED INTEREST IN ACTIVITIES

Frequency: \_ (0-4) Intensity: \_ (0-4)

(9) FEELINGS OF DETACHMENT OR ESTRANGEMENT

Frequency: \_ (0-4) Intensity: \_ (0-4)

(10) RESTRICTED RANGE OF AFFECT

Frequency: \_ (0-4) Intensity: \_ (0-4)

(11) SENSE OF A FORESHORTENED FUTURE

Frequency: \_ (0-4) Intensity: \_ (0-4)

AVOIDANCE/NUMBING INTENSITY AND FREQUENCY SUMS

Frequency: \_ (0-28) Intensity: \_ (0-28)

AVOIDANCE/NUMBING INTENSITY AND FREQUENCY MEANS

Frequency: \_ (0-4) Intensity: \_ (0-4)

CLINICIAN ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

D. PERSISTENT SYMPTOMS OF INCREASED AROUSAL:

(12) DIFFICULTY FALLING OR STAYING ASLEEP

Frequency: \_ (0-4) Intensity: \_ (0-4)

(13) IRRITABILITY OR OUTBURSTS OF ANGER:

Frequency: \_ (0-4) Intensity: \_ (0-4)

(14) DIFFICULTY CONCENTRATING

Frequency: \_ (0-4) Intensity: \_ (0-4)

(15) HYPERVIGILANCE

Frequency: \_ (0-4) Intensity: \_ (0-4)

CLINICIAN ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

D. PERSISTENT SYMPTOMS OF INCREASED AROUSAL:

(16) EXAGGERATED STARTLE RESPONSE

Frequency: \_ (0-4) Intensity: \_ (0-4)

(17) PHYSIOLOGIC REACTIVITY

Frequency: \_ (0-4) Intensity: \_ (0-4)

CLINICIAN ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:

INCREASED AROUSAL INTENSITY AND FREQUENCY SUMS

Frequency: \_ (0-24) Intensity: \_ (0-24)

INCREASED AROUSAL INTENSITY AND FREQUENCY MEANS

Frequency: (0-4) Intensity: (0-4)

OVERALL SYMPTOM INTENSITY AND FREQUENCY SCALES

Frequency: \_ (0-68) Intensity: (0-68) \_

OVERALL SYMPTOM INTENSITY AND FREQUENCY MEANS

Frequency: (0-4) Intensity: (0-4)

CLINICIAN ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:  
CAPS INTERVIEWER RATINGS:

(18) IMPACT ON SOCIAL FUNCTIONING \_ (0-4)

(19) IMPACT ON OCCUPATIONAL FUNCTIONING \_ (0-4)

(20) GLOBAL IMPROVEMENT \_ (0-4)

(21) RATING VALIDITY \_ (0-4)

(22) GLOBAL SEVERITY \_ (0-4)

HYPOTHESIZED OR ASSOCIATED FEATURES:

(23) GUILT OVER ACTS OF COMMISSION OR OMISSION

Frequency: \_ (0-4) Intensity: \_ (0-4)

(24) SURVIVOR GUILT

Frequency: \_ (0-4) Intensity: \_ (0-4)

(25) HOMICIDALITY

Frequency: \_ (0-4) Intensity: \_ (0-4)

(26) DISILLUSIONMENT WITH AUTHORITY

Frequency: \_ (0-4) Intensity: \_ (0-4)  
CLINICIAN ADMINISTERED PTSD SCALE (CAPS-2) SUMMARY:  
HYPOTHESIZED OR ASSOCIATED FEATURES:

(27) FEELINGS OF HOPELESSNESS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(28) MEMORY IMPAIRMENT, FORGETFULNESS

Frequency: \_ (0-4) Intensity: \_ (0-4)

(29) SADNESS AND DEPRESSION

Frequency: \_ (0-4) Intensity: \_ (0-4)

(30) FEELINGS OF BEING OVERWHELMED

Frequency: \_ (0-4) Intensity: \_ (0-4)

CLINICAL GLOBAL IMPRESSIONS:

Severity of Illness: (1-7)

Considering your total-clinical experience with this particular population, how mentally ill is the patient at this time?

- 1=Normal, not at all ill.
- 2=Borderline mentally ill.
- 3=Mildly ill.
- 4=Moderately ill.
- 5=Markedly ill.
- 6=Severely ill.
- 7=Among the most extremely ill patients.

CLINICAL GLOBAL IMPRESSIONS:

Global Improvement: (1-7)

Rate total improvement whether or not, in your judgement, it is due entirely to drug treatment. Compared to his/her condition at baseline, how much has he/she changed?

- 1=Very much improved.
- 2=Much improved.
- 3=Minimally improved.
- 4=No change.
- 5=Minimally worse.
- 6=Much worse.
- 7=Very much worse.

RECEIVED DEC 29 1998

Sertraline (Zoloft)  
NDA 19-839 (S-026)  
Submission Date: October 1, 1998  
Reviewer: Iftexhar Mahmood, Ph. D.

Pfizer, Inc.  
New York, NY 10017  
Received by OCPB: October 13, 1998.  
DEC 28 1998

Review of a Efficacy Supplement

This submission contains efficacy supplement with no pharmacokinetics or biopharmaceutics data. Therefore, no action is necessary on this submission from pharmacokinetics or biopharmaceutics point of view.

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Iftexhar Mahmood, Ph. D.  
Division of Pharmaceutical Evaluation I

RD/FT initialed by Chandra Sahajwalla, Ph. D.  
CC: NDA 19-839 (S-026)  
HFD-120, HFD-860 (Mahmood, Sahajwalla, Mehta), CDR (Barbara Murphy for Drug Files).

TS/ 12/28/98

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EXCLUSIVITY SUMMARY FOR NDA # 19-839

SUPPL # S-026

Trade Name Zoloft Tablets

Generic Name sertraline HCl

Applicant Name Pfizer

HFD # 120

Approval Date If Known \_\_\_\_\_

**PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?**

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

a) Is it an original NDA?  
YES /  / NO /  /

b) Is it an effectiveness supplement?  
YES /  / NO /  /

If yes, what type? (SE1, SE2, etc.) SE1

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

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

\_\_\_\_\_  
\_\_\_\_\_

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

\_\_\_\_\_  
\_\_\_\_\_

d) Did the applicant request exclusivity?

YES /  / NO /  /

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

3 years

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

no

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

YES /  / NO /  /

If yes, NDA # \_\_\_\_\_ Drug Name \_\_\_\_\_

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /  / NO /  /

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

## PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

### 1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /  / NO /  /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# \_\_\_\_\_

NDA# \_\_\_\_\_

NDA# \_\_\_\_\_

**2. Combination product.**

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /  / NO /  /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# \_\_\_\_\_

NDA# \_\_\_\_\_

NDA# \_\_\_\_\_

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

**PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS**

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /  / NO /  /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /  / NO /  /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

\_\_\_\_\_  
\_\_\_\_\_

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /  / NO /  /

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(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /  / NO /

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /  / NO /

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study 640  
Study 671

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

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a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1                      YES /  /                      NO /  /

Investigation #2                      YES /  /                      NO /  /

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

\_\_\_\_\_

\_\_\_\_\_

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1                      YES /  /                      NO /  /

Investigation #2                      YES /  /                      NO /  /

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

Study 640

\_\_\_\_\_

Study 671

\_\_\_\_\_

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

\_\_\_\_\_

\_\_\_\_\_

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

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

Investigation #1  
IND  YES /  / Explain: \_\_\_\_\_  
! NO / \_\_\_ / Explain: \_\_\_\_\_

Investigation #2  
IND #  YES /  / Explain: \_\_\_\_\_  
! NO / \_\_\_ / Explain: \_\_\_\_\_

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

Investigation #1  
YES / \_\_\_ / Explain \_\_\_\_\_ ! NO / \_\_\_ / Explain \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Investigation #2  
YES / \_\_\_ / Explain \_\_\_\_\_ ! NO / \_\_\_ / Explain \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /  /

NO /  /

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_\_  
Signature  
Title: \_\_\_\_\_

\_\_\_\_\_  
Date

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\_\_\_\_\_  
Signature of Office/  
Division Director

\_\_\_\_\_  
Date

cc: Original NDA

Division File HFD-93 Mary Ann Holovac

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**13 Patent and Exclusivity Information**

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**SECTION 13. PATENT AND EXCLUSIVITY INFORMATION**

1. **Active Ingredient:** (1S-cis)-4(3,4-dichlorophenyl)-12,3,4-tetrahydro-N-methyl-1-naphthalenamine hydrochloride
2. **Strength:** 25, 50, and 100mg sertraline
3. **Trade Name:** Zoloft
4. **Dosage Form/Route of Administration:** Tablets/Oral
5. **Application Firm Name:** Pfizer Inc.
6. **NDA Number:** 19-839
7. **Exclusivity Period:** Thirty-six months (3 years) from the date of approval of this supplement to NDA 19-839
8. **Applicable Patent Numbers And Expiration Dates:**  
4,536,518 December 30, 2005  
4,962,128 November 2, 2009  
5,248,699 August 13, 2012

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**14 Patent Certification**

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**SECTION 14. PATENT CERTIFICATION**

Pfizer certifies that patent numbers 4,536,518 (expires December 30, 2005), 4,962,128 (expires November 2, 2009) and 5,248,699 (expires August 13, 2012), which are listed in section 13 of this application, claim, respectively, the drug sertraline, a method of treating anxiety related disorders (including post-traumatic stress disorder) using sertraline, and a crystalline polymorphic form of sertraline hydrochloride, and that sertraline is the subject of this application for approval under section 505 of the Federal Food, Drug, and Cosmetic Act.

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Memo

NDA #: 19-839

Applicant: Pfizer, Inc.

Name of Drug: Zoloft (sertraline)

Indication: Patients with posttraumatic stress disorder

Regarding: Two statistical reviews for sertraline for PTSD

A statistical review dated 22 June 1999 was completed and signed for NDA 19-839. A programming error that affected results given in Tables 4.12 through 4.16 was found, subsequent to the statistical review being entered into the permanent NDA 19-839 file. The statistical reviewer's conclusions about the interpretation of Tables 4.12 through 4.16 were incorrect due to this programming error.

After the error was corrected, Tables 4.12 through 4.16 were updated to reflect the corrected results. Furthermore, Table 4.12 became Table 4.12a, and a new table, Table 4.12b, was created. The conclusions based on the corrected results were also updated.

The statistical review dated and signed off on 27 September 1999 completely supplants the statistical review dated 22 June 1999, even though the statistical review dated 22 June 1999 was signed off and entered into the permanent NDA 19-839 file.

/S/

David Smith, Ph.D.  
Mathematical Statistician

/S/

Concur: Dr. Jin

cc:

Archival NDA #19-839  
HFD-120/Ms. Homonnay-Weikel  
HFD-120/Dr. Hearst  
HFD-120/Dr. Laughren  
HFD-710/Dr. Chi  
HFD-710/Dr. Chen  
HFD-710/Dr. Smith  
HFD-710/Chron

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MEMO OF TELEPHONE CALL

Date: November 30, 1999  
NDA: 20-990  
NDA: 19-839/SE1-026  
Subject: Final labeling for Pending NDA  
Drug: Zoloft (sertraline hydrochloride) tablets (19-839) and oral concentrate (20-990)  
Indication: OCD/Depression/Panic Disorder/PTSD  
Firm: Pfizer  
Contact: Martha Brumfield, Ph.D  
Phone #: (212) 573-5406

At the request of Dr. Laughren, I contacted Dr. Brumfield in reference to their faxed labeling counterproposal dated 11-19-99, responding to the labeling proposal faxed by the Agency on 11-2-99. The labeling revisions reflected changes to the labeling to provide for the new oral concentrate formulation, additional safety related changes previously requested by the Agency or in pending supplemental applications, and corrections to Table 3 in the Adverse Reactions section of labeling. The attempt of these faxes was to secure labeling agreement at the Team leader level.

I informed Dr. Brumfield that the Agency was willing to accept some of Pfizer's proposed changes (see attached e-mail from Dr. Mosholder). Dr. Brumfield was additionally informed that the Agency wished to have a tabular format in lieu of a narrative format for the Adverse Reactions-Sexual Dysfunction section of labeling. Dr. Brumfield replied that Pfizer was willing to accept all of these changes.

I also noted that the PTSD efficacy supplement, 19-839/SE1-026, was to be acted on at the same time as the oral concentrate application, NDA 20-990. Pfizer had previously informed me that they did not wish to have the oral concentrate labeling and the PTSD labeling together for the following reasons: 1) their detail people need to be trained on the appropriate use of the concentrate and the new indication of PTSD, and 2) they are not able to commercially distribute the concentrate until 3/2000.

I informed her that the Agency would be willing to provide separate labeling for the PTSD and the oral concentrate (with the understanding that Pfizer would combine the labeling once the FPL for the oral concentrate was submitted). However, all of the safety related changes in our agreed upon labeling (attached) would also be incorporated into the PTSD labeling so that these changes would be in the marketplace as soon as possible. Dr. Brumfield agreed with this approach.

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ON ORIGINAL

/S/

Paul A. David, R.Ph.  
Regulatory Project Manager

NDA 20-990  
NDA 19-839/SE1-026  
NDA:DIV FILES  
HFD-120/TLaughren/AMosholder  
/PDavid/AMHomonnay  
ATTACHMENTS (2)

NDA 19-839/S-026

*Homonney*

SEP 13 1999

Pfizer Inc.  
Attention: Margaret A. Longshore  
Director  
235 E. 42nd Street  
New York, New York 10017

Dear Ms. Longshore:

We acknowledge receipt of your efficacy supplemental application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Zoloft (sertraline Hydrochloride) Tablets

NDA Number: 19-839

Supplement Number: S-026

Therapeutic Classification: Standard (S)

Date of Supplement: September 10, 1999

Date of Receipt: September 10, 1999

This supplement provides for Zoloft Tablets for the treatment of post-traumatic stress disorder as a new indication.

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on November 10, 1999, in accordance with 21 CFR 314.101(a).

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within 120 days of receipt of your pediatric drug development plan, we will notify you of the pediatric studies that are required under section 21 CFR 314.55.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at [www.fda.gov/cder/pediatric](http://www.fda.gov/cder/pediatric)) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit, and notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Neuropharmacological Drug  
Products, HFD-120  
Attention: Division Document Room  
4008  
5600 Fishers Lane  
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Neuropharmacological Drug  
Products, HFD-120  
Attention: Division Document Room  
4008  
1451 Rockville Pike  
Rockville, Maryland 20852-1420

NDA 19-839/S-026

Page 3

If you have any questions, contact Anna M. Homonnay-Weikel, R.Ph., Project Manager,  
at (301) 594-5535.

Sincerely,

 9/13/89

Russell Katz, M.D.

Acting Director

Division of Neuropharmacological Drug Products

Office of Drug Evaluation I

Center for Drug Evaluation and Research

APPEARS THIS WAY  
ON ORIGINAL

NDA 19-839/S-026

SEP 13 1999

Homonnay

Pfizer Inc.  
Attention: Margaret A. Longshore  
Director, Regulatory Affairs  
235 E. 42nd Street  
New York, New York 10017

Dear Ms. Longshore:

We acknowledge receipt of your September 9, 1999, correspondence notifying us that you are withdrawing your October 7, 1998, supplemental new drug application (NDA) for Zoloft (sertraline hydrochloride) Tablets for the treatment of post-traumatic stress disorder.

Therefore, in accordance with 21 CFR 314.65, this application is withdrawn as of the date of our receipt of your notification, September 9, 1999. This withdrawal does not prejudice any future filing of the application. You may request that the information contained in this withdrawn application be considered in conjunction with any future submission.

If you have any questions, contact Anna M. Homonnay-Weikel, R.Ph., Project Manager, at (301) 594-5535.

Sincerely,

 9/13/99

Russell Katz, M.D.  
Acting Director  
Division of Neuropharmacological Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

47111126

Food and Drug Administration  
Rockville MD 20857

NDA 19-839/S-026

Pfizer Inc.  
235 E. 42nd Street  
New York, New York 10017

OCT 15 1998

Attention: Margaret A. Longshore, Director

Dear Ms. Longshore:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Zoloft

NDA Number: 19-839

Supplement Number: S-026

Date of Supplement: October 7, 1998

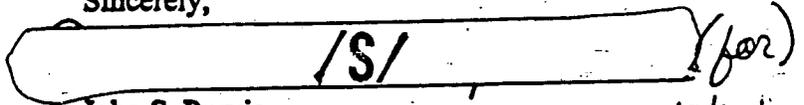
Date of Receipt: October 7, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on December 6, 1998 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research  
Division of Neuropharmacological Drug Products, HFD-120  
Office of Drug Evaluation I  
Attention: Document Control Room 4008  
5600 Fishers Lane  
Rockville, MD 20857

Sincerely,



John S. Purvis  
Chief, Project Management Staff  
Division of Neuropharmacological Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

10/13/98

# PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	<u>19839</u>	Trade Name:	<u>ZOLOFT (SERTRALINE HCL) TABLET</u>
Supplement Number:	<u>26</u>	Generic Name:	<u>SERTRALINE HYDROCHLORIDE</u>
Supplement Type:	<u>SE1</u>	Dosage Form:	<u>Tablet; Oral</u>
Regulatory Action:	<u>AP</u>	Proposed Indication:	<u>post-traumatic stress disorder</u>

### ARE THERE PEDIATRIC STUDIES IN THIS SUBMISSION?

NO, No waiver and no pediatric data

### What are the INTENDED Pediatric Age Groups for this submission?

Neonates (0-30 Days )     Children (25 Months-12 years)  
 Infants (1-24 Months)     Adolescents (13-16 Years)

Label Adequacy	<u>Inadequate for ALL pediatric age groups</u>
Formulation Status	<u>NO NEW FORMULATION is needed</u>
Studies Needed	<u>STUDIES needed. Applicant has COMMITTED to doing them</u>
Study Status	<u>Protocols are under discussion. Comment attached</u>

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

### COMMENTS:

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, ANNA MARIE HOMONNAY-WEIKEL

Signature

[Handwritten Signature]

Date

12-5-99

APPEARS THIS WAY  
ON ORIGINAL