APPENDIX VII: Narratives: Definitive Suicidal Behavior Events: All Non-Depression

The case narratives contained herein reflect non-depression subjects with either definitive suicidal behavior or rating scale emergent suicidal behavior. The case narratives are in the order presented in Table 2.11 of Appendix V.

Protocol Id:	29060 118
Subject Number:	118_003_0155
Case ID:	B0168142A / 1993906067-1
Treatment Group:	Paroxetine
Adverse event Preferred term(s):	Emotional lability; Depersonalization; Emotional Lability
Adverse event Verbatim term(s):	Suicidal gesture; Deralization/suicidal; Deralization/suicidal

Medical Monitor Comments: 26-Apr-1993 (Dr. xxxxxx) Patient in study. Last dose 23-Apr-1993. Last seen 22-Apr-1993. At the time not suicidal but in conflict with ex-husband/live- in boyfriend. Woke 25-Apr-1993 feeling weird - took 6 of boyfriend's pain killers - wanted to cut wrists and took pain killers to numb herself. Drove about 40 miles out of city to country and began laceration of wrist - began to hurt - went to hospital – fell asleep in the parking lot. Woke up in the evening and went home. Called at noon today (26-Apr-1993) to say what she had done. Claims not to be suicidal and feels disturbed about "people in her life pulling her emotionally in different directions." Doubt it's related to medication week 6 study at level 2.

Clinical safety - 27-Apr-1993:
Non-expedite per Clinical Safety Physician.

AE coordinator comments: 29-Apr-1993 (xx)
Per WWCS request: Rx start date = 12-Mar-1993 EST.
Follow-Up Clinical Safety Analyst (xx) Narrative: 30-Apr-1993
Per phone call from Site (study coordinator)
Patient was seen by investigator on 27-Apr-1993 for study discontinuation laboratory work.
Note: Study Med code verified by CRA and Site.
The following changes were made to the "m" page:

- PID# = 18.003.0155
- AE Entry = Suicidal Gesture
- Severity = Sev
- Outcome = Rec
- Onset Date = 24-Apr-1993
- Clear Date = 25-Apr-1993
- Rx Start Date = 12-Mar-1993
- Code added
- Abate = Y
- Inv.Rel. = Probably Unrelated (not Hosp., not life threatening).

Clinical safety - 29-Apr-1993: case maintenance noted; filed.
Clinical safety - 30-Apr-1993
Follow up of 30-Apr-93 reviewed; circulated.

Additional Information:

This 22-year-old female was enrolled in a double-blind clinical study for the treatment of obsessive-compulsive disorder. At the time of study entry, the patient had a diagnosis of obsessive compulsive disorder (DSM-IIIR 300.30). This subject also reported concurrent clinical conditions of tension headaches, hemorrhoids, hayfever, and allergies to molds and grass. Additionally, the patient had a family history of obsessive-compulsive disorder (father).

The subject had previously received treatment with clomipramine for obsessive-compulsive disorder for up to eight weeks with a poor response to treatment. The age when the subject's obsessive-compulsive disorder was diagnosed was 18 years. There were no concurrent medications administered at the time of study entry. It was also noted that the subject was experiencing moderate psychosocial stressors. Obsessions included what the patient did or did not need to do, concern with dirt or other possible contaminations, and concern about doing something embarrassing. Compulsions included dressing rituals, washing rituals, and checking locks.

The subject had no documented history of suicidal thoughts, suicide attempt or self-harm at the time of study entry. The screening and randomization scores on HAMD items #3, reflecting suicidality, were both 0, and the total HAMD-17 and HAMD-21 at randomization were 11 and 14, respectively.

Forty-four days after the first dose of study medication, paroxetine, and while receiving level 2 dosing per protocol, the subject experienced suicidal ideation and engaged in the suicidal gesture described above. The subject also reported the non-serious event of derealization in the setting of the events. All of the events were assessed by the investigator as severe in intensity and probably unrelated to study treatment.

At the time of the adverse events, the subject was one day post cessation of study treatment. Study treatment was discontinued and the subject was withdrawn from the study.

During the course of the double-blind phase of the study and while receiving paroxetine, the subject also experienced the following non-serious adverse events provided with the corresponding intensity and relationship to study medication assessments by the investigator: anxiety (mild, probably related), delayed orgasm (moderate, probably related), headache (mild, probably unrelated), shakiness/tremors (mild probably related), breast soreness (mild, probably unrelated), headache (mild, probably unrelated), which commenced one, three, 15, 15, 19, and 28 days after the first dose of study medication, respectively. The anxiety resolved the same day of onset and the diarrhea resolved

during the course of the study. The headache and delayed orgasm resolved three days after study treatment, and the event of mind racing remained unresolved at the end of study treatment.

Observed efficacy scores by study week for the subject are listed below.

HAMD

Day of HAMD Visit	HAMD item 3: suicide	HAMD: Weighted Total score (17 items)	HAMD: Weighted Total score (21 items)
-13	0	11	14
0	0	8	10
47	3	18	20

Symptom Checklist SCL-90

Day of Visit	Thoughts of Ending Your Life	Thoughts of Death or Dying
-13	0	0
0	0	0
29	0	0

Protocol Id:	120
Subject Number:	120_011_0065
Treatment Group:	Paxil
Adverse event Preferred term(s):	Emotional lability
Adverse event Verbatim term(s):	Suicidal thoughts

This 20-year-old female was enrolled in a double-blind clinical study for the treatment of panic disorder. At the time of study entry, the patient had a diagnosis of panic disorder according to DSM-IIIR criteria. This subject also reported concurrent clinical conditions of frequent headaches, migraines, sometimes feeling nauseated for 1-2 hours after eating, very mild asthma, hives secondary to allergies, and allergic reactions to everything tested, including penicillin. Additionally, the patient had a history of a suspected episode of major depression and suspected dysthymic disorder.

The subject reported that she had received no previous treatment for panic disorder. The approximate time since the first appearance of symptoms of panic disorder was five years and 10 months, and concurrent medications reported at the time of study entry included ibuprofen, acetylsalicylic acid, and paracetamol, all on an as needed basis. It was also noted that the subject was unemployed at the time of study entry and was avoiding going out of the house at all.

The subject had a documented history of previous suicidal thoughts and suicide attempt at the time of study entry. She had attempted to commit suicide at the age of 13 by overdose. The randomization score on MADRS item #10, reflecting suicidality, was 2 and the total MADRS scores at randomization was 22.

Seventeen days after the first dose of study medication (Paxil), the subject experienced increased feelings of a depressed mood, which was assessed as mild in intensity and unassessable in relation to study medication by the investigator. Seven days after this event, the subject experienced increased suicidal thoughts. Study medication had been discontinued one day prior to this second event due to lack of efficacy and the subject's use of marijuana and hashish. She had deteriorated markedly since beginning study treatment and was experiencing increased feelings of depressed mood. On the day of the event of increased suicidal thoughts, the subject wrote a long detailed suicide note to her parents and then disappeared. She was picked up by police later that day and was involuntarily admitted to the psychiatric ward of a local hospital. The investigator assessed the event as severe in intensity and unrelated to study medication. At the time of the final study follow-up, the event was considered resolved.

At the time of the adverse events described above, the subject was receiving Paxil, 40mg/day. During the course of her hospitalization the study medication was discontinued and Paxil was subsequently reintroduced at a dose of 10 mg/day. It was noted that she was continued on this treatment. Reported concomitant medications at the

time of the adverse event included ibuprofen, acetylsalicylic acid, and paracetamol, all of which were recorded as being used on an as needed basis.

During the course of the double-blind phase of the study, the subject also experienced decreased appetite, nausea, headache, hypertension and postural hypotension, commencing 7, 7, 7, 12, 23, and 23 days after the first dose of study medication (Paxil), respectively. All of these events resolved over the course of the study.

Observed efficacy scores by study week for the subject are listed below.

	MADRS	
Day of MADRS Visit	MADRS item 10: suicide	MADRS total
0	2	22

Protocol Id:	29060 136
Subject Number:	136_067_0403
Treatment Group:	Paxil
Adverse event Preferred term(s):	Depression, Emotional Lability
Adverse event Verbatim term(s):	Major Depressive State of Severe Intensity, Suicide Attempt

51 YEAR OLD FEMALE PATIENT, ATTEMPTED SUICIDE ON 23 AUG 1993 BY INGESTION OF
10 TABLETS OF ROHYPNOL (FLUNITRAZEPAM) 2 MG.SHE WAS SEVERLY DEPRESSIVE,WITH CONCENTRATION DISORDER.
FURTHER INFORMATION AS SOON AS AVAILABLE
UPDATE 30 AUG 1993:
THE PATIENT PRESENTED WITH OBSESSIVE COMPULSIVE DISORDERS FOR MORE THAN 10
YEARS. SHE WAS ALREADY HOSPITALIZED IN 1990 FOR SEVERE DEPRESSION.
THE SUICIDAL IDEAS OF THE PATIENT DECREASED, BUT SHE IS STILL HOSPITALIZED.

Additional Information:

This 51-year-old female was enrolled in a double-blind clinical study for the treatment of obsessive-compulsive disorder. At the time of study entry, the patient had a diagnosis of obsessive-compulsive disorder according to DSM-IIIR criteria. This subject also reported concurrent clinical conditions of menopause, presbyism and obesity.

The subject had previously received treatment with amitriptyline hydrochloride, prior to investigational study, for obsessions. Efficacy and tolerability were unknown. Treatment with amitriptyline hydrochloride was discontinued 14 days prior to treatment with investigational product. The subject presented with obsessive-compulsive disorder for more than 10 years. Concurrent medication administered at the time of study entry was reported as chloral hydrate. It was also noted that the subject was experiencing the following obsessions and/or compulsions at the time of study recruitment: fear of harming self, fear of harming others, fear of blurting out obscenities or insults, concerns or disgust with bodily waste or secretions, forbidden or perverse sexual thoughts, images, or impulses, aggressive sexual behaviour toward others, concern with objects of monetary or sentimental value, concerns with sacrilege and blasphemy, obsessions with a need for symmetry or exactness accompanied by magical thinking, a need to know or remember, a fear of not saying just the right thing, a fear of losing things, obsession with intrusive nonsense sounds, words or music, superstitious fears, concern with illness or disease, excessive concern with body part or an aspect of appearance, compulsions with

taking measures to prevent or remove contact with contaminants, checking locks, stove, appliances, etc, checking that she did not make a mistake, checking that no one broke into house, compulsions with re-rereading or re-writing, ordering and arranging, excessive list-making, the need to tell, ask or confess, measures to prevent harm to self and harm to others, and superstitious behaviours.

The subject had no documented history of suicidal thoughts, suicide attempt or self-harm at the time of study entry. The screening and randomization scores on MADRS item #10 reflecting suicidality were both 0, and the total MADRS score at randomization was 13.

Forty-three days after the first dose of study medication, Paxil, the subject experienced a major depressive state of severe intensity which was assessed as serious, severe in intensity and probably related to study medication by the investigator. She was observed to be tense, anxious and sad, with a lack of concentration. One day later and 44 days after the first dose of study medication, the subject attempted suicide which was assessed as serious, severe in intensity and related to study medication. The subject impulsively took 10 tablets of Rohypnol 2mg. The subject was hospitalized due to both of these adverse events.

At the time of the adverse events, the subject was receiving Paxil at dose level 4 (dosing ranges for Paxil were 10-60mg/day). Reported concomitant medications taken at the time of the adverse events included chloral hydrate.

Treatment with study medication was discontinued 44 days after the first dose and the subject was withdrawn from the study.

The first day of treatment with study medication, Paxil, the subject was noted to have a 3.5kg weight loss. Eight days later, the event was assessed as resolved. During the double-blind phase of the study and while receiving paroxetine at dose level 1, the subject experienced hot flushes and loss of weight four and nine days respectively, after the first dose of study medication. Both events remained ongoing at the end of study treatment. While receiving paroxetine at dose level 3, the subject experienced pain in the chest and nausea 28 days after the first dose of study medication. These events also remained ongoing at the end of study treatment.

Additionally, during the double-blind phase of the study and while receiving Paxil at dose level 1, the subject experienced akathisia nine days after the first dose of study medication. While receiving Paxil at dose level 3, the subject developed tremors 28 days after the first dose of study medication. Both events were ongoing at the end of study treatment.

The subject did not complete the study and did not continue into long-term therapy.

Observed efficacy scores by study week for the subject are listed below.

MADRS

Day of MADRS Visit	MADRS item 10: suicide	MADRS total*
-14	0	13
0	0	13
9	1	16
13	0	19
20	1	19
28	2	20
44	6	46

Protocol Id:	136.067.0436
Subject Number:	136.067.0436
Treatment Group:	Placebo
Adverse event Preferred term(s):	Emotional lability
Adverse event Verbatim term(s):	Suicide attempt by drugs

A 53 year old patient, treated for obsession-compulsive disorder since an unknown date. She entered the 136 study 0n 19 August 1993, and began medication on 03 Sep 93. She experienced a suicide attempt 06 September 1993, by ingestion of study drug and perhaps some other unknown antidepressant. She was hospitalized in intensive care unit, where she presented confusion, a tachycardia (100-105/min), and an atropinic syndrome. The ECG was normal. A washing out of stomach and research of imipramine was undergone, but blind was not broken. Initial outcome is favorable, but patient is still hospitalized and not yet recovered.
Update 07-Sep-93:
Patient presented with an obsessional neurosis for 20 years.
She ingested the whole content of the study drug supply (16 tablets), and the rest of a laroxyl package (number of tablets unknown).
Update 27 Sep 1993:
After review of the case by the reporter, it has been confirmed that the patient attempted suicide by intentional ingestion of 3 tablets of the study drug (and not 16 as previously reported), and 10 tablets of clomipramine 75 mg (and not laroxyl, as previously reported). Following reporter, the AE is probably related to the study drug.

Additional Information:

This 53-year-old female was enrolled in a double-blind clinical study for the treatment of obsessive-compulsive disorder (OCD). At the time of study entry, the patient had a diagnosis of obsessive-compulsive disorder (DSM-IIIR: 300.40). This subject also reported concurrent clinical conditions of hypoacousia, presbyopia, allergic rhinitis, headache, and insomnia. The screening physical exam revealed that the subject had myopia.

The subject reported that she had received previous drug therapy for OCD, but it was neither adequate nor efficacious. The subject was diagnosed with OCD in 1973, approximately 19 years prior to study entry, and concurrent medications recorded at the time of study entry included paracetamol, mequitazine, and chloral hydrate.

The subject had no documented history of suicidal thoughts, suicide attempt or self-harm at the time of study entry. The screening and randomization scores on MADRS item #10, reflecting suicidality, were both 0, and the total MADRS score at randomization was 6.

One day after the first dose of study medication (placebo), the subject became aggressive and agitated, and two days later, she attempted suicide by impulsively ingesting three

capsules of study medication (placebo) and ten capsules of clomipramine (750 mg). Three hours after the ingestion, she was admitted to the intensive care unit of the hospital, where she presented with confusion, tachycardia (100-105 beats/min) and an "atropinic syndrome" (anticholinergic syndrome). Gastric lavage was carried out. Her EKG and lung radiography were normal, and lab values did not show any abnormalities, except hypokalemia on the check up done after the gastric lavage, which was recorded later as reverting to normal. The investigator assessed the event as serious, severe in intensity and probably related to study medication. The subject was discharged from the hospital after three days, and the event was considered resolved.

At the time of the adverse event, the subject was receiving placebo at a dose equivalent to Paxil at Dose level 1 per protocol (active study treatment involved flexible dosing of Paxil 10-60mg/day and clomipramine 25-250mg/day). Concomitant medications taken at the time of the adverse event included paracetamol, mequitazine, and chloral hydrate.

Study medication was discontinued on the day of the event, and the subject was withdrawn from the study due to significant adverse events.

It was noted that the toxicology screening was totally negative (blood and gastric lavage fluid), which cast doubt on the diagnosis of drug intoxication.

One day after study medication was discontinued a repolarization disorder was detected on the subject's EKG. The investigator assessed the event as mild in intensity and unrelated to study medication, and the event was considered unresolved at the time of the final study follow-up.

Observed efficacy scores by study week for the subject are listed below.

MADRS

Day of MADRS Visit	MADRS item 10: suicide	MADRS total
-14	0	7
0	0	6

Protocol Id:	187.035.0510
Subject Number:	187.035.0510
Treatment Group:	Placebo
Adverse event Preferred term(s):	Emotional lability
Adverse event Verbatim term(s):	Pseudo tendamen suicidii

This 37-year-old male was enrolled in a double-blind clinical study for the treatment of panic disorder. At the time of study entry, the patient had a diagnosis of panic disorder with agoraphobia, per DSM-IIIR criteria. This subject also reported concurrent clinical conditions of allergic reactions. Additionally, the subject had a history of 12 episodes of panic disorder with agoraphobia, and the average duration of each episode was 26 weeks. The subject also reported a suspected episode of major depression in 1989.

The subject was previously treated with prothiaden for his panic disorder which was ineffective. The most recent episode of panic disorder was of six months duration and no concurrent medications were reported at the time of study entry.

The subject had no documented history of suicidal thoughts, suicide attempt or self-harm at the time of study entry. The screening and randomization scores on MADRS item #10 reflecting suicidality were both 1, and the total MADRS score at randomization was 20.

Fifty-nine days after the first dose of study medication (placebo), the subject attempted suicide with an intentional overdose of barbital. The subject reportedly had begun drinking after his last study visit, 17 days prior to the event, and his drinking had accelerated. On the day of the event, the subject ingested 3750 mg of barbital. The subject was admitted to a local mental hospital on the day of the event, study medication was discontinued, and the subject was withdrawn from the study. The investigator assessed the event as severe and unrelated to study medication. The event was resolved within one day.

At the time of the adverse event, the subject was receiving placebo at a dose equivalent to the medium dose level of Paxil or clomipramine. Concomitant medication at the time of the event was barbital. Of note, study drug had been titrated up as per protocol during the first four weeks of the study. Twenty-nine days after the first dose of study medication (placebo), the subject's dose was titrated up to the highest level of study medication due to desire for better effect. However, the dosage was titrated back down to the medium dose level one day later due to side effects.

During the course of the double-blind phase of the study, the subject also experienced headache, sweating, and nausea which commenced 31, 31, and 32 days after the first dose of study medication. It was unknown if the events were continuing at the time of study termination.

Observed efficacy scores by study week for the subject are listed below.

MADRS

Day of MADRS Visit	MADRS item 10: suicide	MADRS total*
-21	1	23
0	1	20
21	0	14
42	0	12

Protocol Id:	29060 187
Subject Number:	187.011.0531
Treatment Group:	Placebo
Adverse event Preferred term(s):	Emotional lability
Adverse event Verbatim term(s):	Suicide attempt

This 36 year old male patient was taking part in paroxetine study 187 suffering from panic disorder. The patient felt superficially better during the placebo run-in period but had suicidal impulses when under the influence of alcohol. After drinking beer at home on day 2 of receiving study medication (placebo), he felt restless and desperate. He took Sobril (75 mg), Trilafon (48 mg) and Rinexin (12 mg) after which he immediately informed his wife who took him to hospital. The patient underwent lavage. He felt well the following day and was no longer suicidal. The event is reported to be probably unrelated to the study therapy.

Additional information:

This 35-year-old male was enrolled in a double-blind clinical study for the treatment of panic disorder. At the time of study entry, the patient had a diagnosis of panic disorder with agoraphobia per DSM-IIIR criteria. The severity was considered to be mild for agoraphobic avoidance. This subject also reported a concurrent clinical condition of a cartilage problem in both knees and an allergy to penicillin and an allergy to perfume (resulting in respiratory distress). Additionally, the patient had a previous history of a major episode of depression as well as a brief episode of depression. The subject also reported a familial disposition to panic disorder.

At study entry the subject had not previously had an episode of panic disorder or received treatment for panic disorder. The panic disorder with agoraphobia for which the subject was enrolled in the study was the subject's first episode and was of ten years in duration. Just prior to study entry he was treated with perphenazine as well as an additional unidentified agent that was stopped prior to study entry due to restlessness and anxiety.

The subject had no documented history of suicidal thoughts, suicide attempt or self-harm at the time of study entry. The randomization and baseline scores on MADRS item #10, reflecting suicidality, were 2 and 0, respectively, and the total MADRS score at randomization was 13.

Thirty five days after the first dose of study medication, placebo, the subject attempted suicide by taking oxazepam 75 mg, perphenazine 48 mg, and phenylpropanolamine 12 mg. The event was assessed by the investigator as moderate in intensity and probably unrelated to study treatment. The subject had been drinking on the evening of the event and felt restless and desperate. After taking the medications he immediately informed his wife. He was taken to the hospital for treatment where he underwent gastric lavage.

Treatment with study medication was continued. He felt fine afterwards, with no suicidal thoughts, and the event was considered resolved the following day. At the time of the event, the subject was receiving placebo at a dose equivalent to Paxil at the low dose level. No concomitant medications were taken at the time of the adverse event.

During the double-blind phase of the study, 13 and 43 days after the first dose of study medication, the subject developed two episodes of irritability (both of mild intensity and considered unassessable by the investigator). At the time of the first episode he was receiving placebo at a dose equivalent to Paxil at the low dose level. During the second episode he received placebo at a dose equivalent to Paxil at the high dose level. Fifty eight days after the first dose of study medication, while continuing on placebo at a dose equivalent to Paxil at the high dose level, he developed sweating (moderate intensity, probably related). The sweating resolved in three weeks however the irritability was unresolved at the end of the study.

The subject completed the study per protocol.

Observed efficacy scores by study week for the subject are listed below.

MADRS

Day of MADRS Visit	MADRS item 10: suicide	MADRS total
-21	2	23
1	0	13
26	2	25
48	1	19
93	0	10

Protocol Id:	502.045.05077
Subject Number:	502.045.05077
Treatment Group:	Placebo
Adverse event Preferred term(s):	Emotional lability
Adverse event Verbatim term(s):	Overdose (intentional)

Case reference number 97001261-1 is a clinical trial report from blinded study 29060/502. The 34 year old male patient received study medication from 14-Jan-97 for depression.
The patient had a medical history of deep vein thrombosis (1993) but had not been receiving warfarin 'for some months'. The patient gradually developed insomnia (no particular date of onset).
The patient took an overdose of study medication (placebo), benzodiazepine (diazepam), chloral hydrate and possibly warfarin and on 18-Jan-97 (03:00hrs). The patient received no treatment for the event. It was reported that the patient became frustrated from lack of sleep and thought that the medication was not effective.

Study medication was recored as having stopped on 18-Jan-97 and the patient was admitted to a general hospital on the same day (intensive care unit). He remains hospitalised in a psychiatric hospital. The randomisation code was broken by the investigator.
The investigator considered the event to be possibly related to the study medication. It was also stated to be possibly related to the conduct of the study and the patient's primary condition.
OVERDOSE

Additional Information

This 34-year-old male was enrolled in a double-blind clinical study for the treatment of social phobia. At the time of study entry, the patient had a diagnosis of social phobia, per DSM-IV criteria. This subject reported no concurrent clinical conditions. Additionally, the subject had a history of depression (DSM-IV: 293.33).

The subject reported previously receiving treatment with venlafaxine hydrochloride, clotiapine, fluvoxamine maleate, thioridazine, flunitrazepam, alprazolam, zopiclone, diazepam, chloral hydrate, Paxil, chlorpromazine hydrochloride, trimipramine, and trihexyphenidyl hydrochloride. The length of time that the subject had social phobia was of more than three year’s duration, and concurrent medication reported at the time of study entry was chloral hydrate.

Five days after the first dose of study medication (placebo), the subject experienced a sudden onset of depression and engaged in an intentional overdose of study medication and other medications at his disposal, including diazepam, chloral hydrate, and possibly warfarin. The subject had become frustrated from lack of sleep and thought that the study medication was not effective. The subject was admitted to the psychiatric hospital on the same day as the event. The investigator assessed the event as serious, severe in intensity and possibly related to study medication, and to also be possibly related to the conduct of the study and the patient's primary condition.

At the time of the adverse event, the subject was receiving placebo at a dose equivalent to Paxil, 20 mg/day. Concomitant medication at the time of the event was chloral hydrate. Of note, the subject was experiencing severe insomnia at the time of the event.

Treatment with study medication was discontinued on the day of the event, and the overdose was considered resolved after 24 hours. The subject was discharged from the hospital, but had been lost to follow-up after termination from the study.

Protocol Id:	502.037.05146
Subject Number:	502.037.05146
Treatment Group:	Paroxetine
Adverse event Preferred term(s):	Emotional Lability
Adverse event Verbatim term(s):	Suicide

Case reference 97017163-1 is a clinical trial report from study 29060 502 which is a double blind study referring to a male patient aged 23 years.

On the 10 June 1997, the patient started taking study medication for social phobia. The patient failed to present for a scheduled appointment on 15 July 1997; the investigator was later informed that the patient committed suicide on 14 July 1997.

According to the patient's mother, the patient had stolen a large amount of his grandmother's medication (bisporolol hemifumarate, isosorbide dinitrate, nitrazepam). An autopsy has been refused by the patient's parents.

The investigator considered that the events were probably unrelated to study medication and could possibly be associated with the patient's primary condition.

Additional Information

This 23-year-old male was enrolled in a double-blind clinical study for the treatment of social phobia. At the time of study entry, the patient had a diagnosis of social phobia, per DSM-IV criteria. This subject reported no concurrent clinical conditions at the time of study entry. Additionally, the patient had a previous history of avoidant personality disorder (DSM-IV: 301.82).

The subject reported no previous pharmacotherapy treatment in the last year for social phobia; however, he was receiving psychotherapy at the time of study entry. The length of time that the subject had social phobia was of more than three year's duration, and no concurrent medications were reported at the time of study entry.

Thirty-five days after the first dose of study medication (Paxil), the subject committed suicide. According to the patient's mother, the patient stole a large amount of his grandmother's medication (bisporolol hemifumarate, isosorbide dinitrate, nitrazepam). An autopsy was refused by the patient's parents. The investigator assessed the event as serious, severe in intensity, and probably unrelated to study medication and could possibly be associated with the patient's primary condition.

At the time of the adverse event, the subject was receiving Paxil, 40 mg/day. There were no concomitant medications reported at the time of the event.

During the course of the double-blind phase of the study, while receiving Paxil, 20 mg/day, the subject also experienced a heavy feeling on his eyes. This event commenced nine days after the first dose of study medication, and resolved after 13 days.

Protocol Id:	29060 502
Investigator Number:	
Patient Number:	502.003.05511
Treatment Number:	00048
Case Id:	B0205845A / 1997020165-1
Suspect Drugs:	Paroxetine hydrochloride, Paroxetine hydrochloride, Paroxetine hydrochloride, Paroxetine hydrochloride
Serious Events:	Intentional misuse

Case reference 97020165-1 is a clinical trial report from blinded study 29060/ 502. The 19 year old male patient began receiving study medication from 11-Jun-97 for social phobia.

On the 19-Aug-97 at approximately 24:00 hrs, the patient intentionally took an overdose of study medication (possibly 19 blue capsules). The background is as follows:
The patient was having problems with his new job and on the 12-Aug-97, he resigned because of stress. On the 19-Aug-97, he was contacted and told that he owed his employers money. The patient reacted unfavourably, he became stressed and depressed. On the days preceeding the overdose, he execesively consumed both alcohol and cannabis.

On the night of the overdose, he was intoxicated, due to the consumption of alcohol and cannabis, to the point of memory loss. He remembers feeling 'low' and having a 'want to die'. He wrote several suicide notes and took his study medication before loosing conciousness. On the 19-Aug-97, he tried to overdose by consuming paracetamol and aspirin in a deliberate effort to cause himself injury. In the morning of the 20-Aug-97, his mother failed to wake him and consequently phoned the ambulance.

He was briefly monitored on the ward, but he was fit for discharge at midday on the 20-Aug-97. He was examined by a psychiatrist who noted that he no longer exhibited suicidal tendancies.

He was examined by the investigator on the 21-Aug-97 and he was in agreement with the oncall psychiatrist. The patient still had the longstanding problems with isolation, motivation and 'adolescent issuses'. The patient received his last dose of study medication on 19-Aug-97.

The investigator considered the events to be probably unrelated to the study medication and may be associated to social phobia.

Additional Information

Protocol Id:	502.003.05511
Subject Number:	502.003.05511
Treatment Group:	Paroxetine
Adverse event Preferred term(s):	Emotional lability
Adverse event Verbatim term(s):	Overdose

This 20-year-old male was enrolled in a double-blind clinical study for the treatment of social phobia. At the time of study entry, the patient had a diagnosis of social phobia, per DSM-IV criteria. This subject reported no concurrent clinical conditions.

The subject reported no previous treatment for social phobia. The length of time that the subject had social phobia was of more than three year's duration, and no concurrent medications were reported at the time of study entry.

Seventy days after the first dose of study medication (Paxil), the subject intentionally took an overdose of study medication (possibly 19 blue capsules), acetylsalicylic acid and paracetamol. The patient had problems with his new job and, seven days prior to the event, he resigned because of stress. On the day of the event, he was contacted by his former employer and told that he owed them money. The patient reacted unfavourably, and became stressed and depressed. In the days preceding the overdose, he excessively consumed both alcohol and cannabis.

On the night of the overdose, he was intoxicated, due to the consumption of alcohol and cannabis, to the point of memory loss. He remembers feeling 'low' and 'want to die'. He wrote several suicide notes and took his study medication before losing consciousness. He tried to overdose by consuming paracetamol and aspirin in a deliberate effort to cause himself injury. On the morning after the overdose, his mother failed to wake him and consequently phoned the ambulance.

He was briefly monitored on the ward, but he was fit for discharge at midday on the same day he was admitted. He was examined by a psychiatrist who noted that he no longer exhibited suicidal tendencies.

He was examined by the investigator two days after the event and he was in agreement with the on-call psychiatrist. The patient still had the longstanding problems with isolation, motivation and 'adolescent issues'.

The investigator considered the events to be serious, moderate in severity, probably unrelated to the study medication, and may be associated to social phobia.

At the time of the adverse events, the subject was receiving Paxil, 50 mg/day. There was no concomitant medication at the time of the event.

Treatment with study medication was discontinued on the day of the event, and the overdose was considered resolved after one day. The subject was withdrawn from the study on the day after the event.

As described above, the subject experienced stress, depression, alcohol abuse, and cannabis abuse during the course of the study, while receiving Paxil, 50 mg/day. The events commenced 69, 69, 70, and 70 days, respectively, after the first dose of study medication. The investigator assessed the stress, alcohol and cannabis abuse as moderate in severity and probably unrelated to study medication; and the depression was assessed as mild in severity and probably unrelated to study medication. Each event was considered resolved at the time of study termination.

During the course of the double-blind phase of the study, on the day that Paxil, 20 mg/day was initiated, the subject experienced nausea and sleepiness. Both events resolved over the course of the study.

Protocol Id:	29060 627
Subject Number:	627.100.01028
Treatment Group:	Paxil
Adverse event Preferred term(s):	Depression, Emotional lability
Adverse event Verbatim term(s):	Severe Depression; Suicidal; overdose of Loramet

Case reference number 1998023695-1 is a clinical trial report from blinded study 29060/627 for post-traumatic stress disorder. This report refers to a 27-year-old male (patient identification number 627.603.01028).

The patient received oral study medication from 02 September 1998. On 05 September 1998, some 4 days after the first dose, the patient was severely depressed and suicidal following a break up of his relationship, an unwelcome move at work and an argument with his mother, where she accused him of causing a rift in her relationship with his father. At 21:30 hours, the patient took an overdose of unknown tablets (possibly Lasamet). The patient experienced drowsiness for approximately 24 hours following the overdose. The patient did not receive corrective therapy.

Treatment with study medication was stopped due to this event and the patient took the last dose on 04 September 1998. The patient recovered from the overdose on 05 September 1998 but had not recovered from the severe depression. The investigator considered the depression, suicidal ideation and overdose as serious because they were life threatening and resulted in prolonged hospitalisation of the patient.

The investigator considered the depression, suicidal ideation and overdose as unrelated to treatment with study medication. The investigator considered the events could be associated with the patient's primary condition; post-traumatic stress disorder.

OVERDOSE

Additional information:

This 27-year-old male was enrolled in a double-blind clinical study for the treatment of post-traumatic stress disorder. At the time of study entry, the patient had a diagnosis of post-traumatic stress disorder, according to DSM-IV criteria. This subject reported no concurrent clinical conditions and no previous psychiatric history. The subject previously received treatment with nefazodone within the three months prior to study entry.

The post-traumatic stress, for which the subject was enrolled in the study, resulted from his experience in the course of his police duties during gang wars. He was raped by car highjackers, forced to participate in post-mortems on traumatized children, and exposed to violence and death. No concurrent medications were administered at the time of study entry.

The subject had no documented history of suicidal thoughts, suicide attempt or self-harm at the time of study. The baseline score on MADRS item #10, reflecting suicidality, was 1, and the total MADRS score at baseline was 37.

Four days after the first dose of study medication, Paxil, the subject experienced severe depression and became suicidal (as described above). He subsequently took an overdose of Loramet and was hospitalized. The investigator assessed the events as severe and unrelated. At the time of the adverse events, the subject was receiving Paxil at a dose of 20 mg/day. No concomitant medications were reported being taken at the time of the adverse events. Treatment with study medication was discontinued and the subject was withdrawn from the study. The overdose was considered resolved the same day. The outcome of the suicidal depression was unknown at the end of the study as the subject was lost to follow-up.

Observed efficacy scores by study week for the subject are listed below.

MADRS

Day of MADRS Visit	MADRS item 10: suicide	MADRS total*
0	1	37

Protocol Id:	29060 660
Subject Number:	660.23502
Treatment Group:	Paxil
Adverse event Preferred term(s):	Suicide Attempt
Adverse event Verbatim term(s):	Intentional Overdose

Case reference number 2001009212-1, is a clinical trial report from blinded study 29060/660 for obsessive compulsive disorder. This report refers to a 16-year-old female (patient identification number 660.235.23502).

The patient's medical history included suicidal ideation. Concomitant medications included clotiazepam (Rize) and flunitrazepam (Silace).

The patient received oral study medication from 23 March 2001, following a placebo run-in phase. On 10 April 2001, 18 days after the first dose, the patient took ten days supply of study medication and the equivalent amount of clotiazepam (50 mg) and flunitrazepam (15 mg) at the same time. The patient's family made the patient vomit and the tablets could be seen. The patient fell asleep following the vomiting episode. On 11 April 2001, the patient awoke with a headache which the investigator considered to be non-serious and was reported to have improved later the same day. The patient was not treated for the overdose. The investigator initially considered the final diagnosis to be worsening suicidal ideation and intentional overdose. The investigator reported that the patient had a difficult family background. The investigator later reported that the initial report of suicidal ideation was not a serious adverse event and that upon further investigation the patient was assessed to have performed an act of self-harm.

Treatment with study medication was stopped on 11 April 2001, the patient received the last dose on 09 April 2001. The headache resolved on 20 April 2201. The investigator considered this to be a serious event because the patient experienced an overdose.

The investigator reported the overdose to be probably unrelated to treatment with study medication.

Additional Information:

This 16-year-old female was enrolled in a double-blind clinical study for the treatment of obsessive compulsive disorder (OCD). At the time of study entry, the patient had a diagnosis of obsessive compulsive disorder per DSM-IV criteria. This subject reported the concurrent clinical condition of adjustment disorder. Additionally, she had a history of sleep disorder and her premorbid character was described as strong hysteria.

The subject had previously received treatment with brotizolam and flunitrazepam with unknown efficacy and tolerability. The subject began exhibiting signs of OCD

approximately seven months prior to study enrollment, and her obsessions included fear that she might injure others, an obsession with contamination of animals and fermented soybeans, and a fear of sharp ends. Her compulsions included urinary frequency, compulsive hand washing, arranging and organizing objects, fasting doors, and shutting off gas valves. She had no deliberate avoidance tendency. Concurrent medications administered at the time of study entry were reported as clotiazepam and flunitrazepam. It was also noted that the subject had a difficult family background at the time of study entry.

The subject had no history of suicidal ideation at the time of study recruitment. The screening and randomization scores on HAMD item #3 reflecting suicidality were both 1, and the total HAMD score at randomization was 12.

Twenty days after the first dose of study medication (Paxil IR), the subject took a ten day supply of study medication and the equivalent amount of clotiazepam (50 mg) and flunitrazepam (15 mg) at the same time. The subject's family made her vomit and the tablets were visualized. The subject fell asleep following the vomiting episode. The investigator assessed the event as serious, of moderate intensity, and of unlikely relationship to study medication. The event was considered resolved within one day. Later on the day of the event, the subject awoke with a headache which the investigator considered to be of moderate intensity and of unlikely relationship to investigational product. This event resolved after one day.

The investigator initially considered the final diagnosis to be worsening suicidal ideation and intentional overdose. The investigator reported that the subject had a difficult family background. The investigator later reported that the initial report of suicidal ideation was not a serious adverse event and that upon further investigation the subject was assessed to have performed an act of self-harm.

At the time of the adverse events, the subject was receiving Paxil IR at a dose of 40 mg/day. Reported concomitant medications being taken at the time of the adverse events included the aforementioned medications. It was also noted that, at the time of the events, the subject was living in a complicated family environment as well as in a situation that would easily cause an in-family conflict due to the change of the house immediately before the start of the study.
Treatment with study medication was discontinued on the same day as the event and the subject began treatment with Paxil.
Observed efficacy score per study week for the patient are listed below.

	HAMD	
Day of HAMD visit	HAMD #3 suicide	HAMD-17 total
Day -7	1	14
Day 1	1	12
Day 20	3	18